A study of variability predictors and clinical features of treated incidence of schizophrenia in Riyadh, Saudi Arabia

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A study of variability predictors and clinical features of treated incidence of schizophrenia in Riyadh, Saudi Arabia

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DEDICATION

This thesis is dedicated to the soul of my Mom, my beloved Father, and my two beloved kids; Sara and Alwaleed for their endless love, support and encouragements.

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A study of variability predictors and clinical features of treated incidence of schizophrenia in Riyadh, Saudi Arabia

ABSTRACT

This Ph.D. thesis is presented as three separate papers, and the overall aim of this research is to describe and achieve a broader and clearer understanding of the epidemiology, aetiology and symptomatology of schizophrenia in Saudi Arabia. The first study provides knowledge about the epidemiology of schizophrenia by investigating the incidence in Riyadh, Saudi Arabia and using the incidence data to describe heterogeneity across districts in Riyadh. In addition, the study tests whether variation in incidence occurs according to nationality, sex, age, marital status, employment status, and income. The second study evaluates the five-factor model in Saudi schizophrenia patients by factor analysis of OPCRIT items as rated from the health records. It also tested whether there was any association between the five factors and demographic data included in OPCRIT. The third study describes the duration of untreated psychosis in Riyadh to identify any association between both patient demographic factors and their first pathway to care with their duration of untreated psychosis (DUP). The chosen study design for the whole research was a retrospective case note study of all incident cases of schizophrenia over a 2 years period presenting in the capital city of Saudi Arabia. The first study is an epidemiological study with an ecological design, which determines the incidence of schizophrenia amongst the population in Riyadh and to identify associations between incidence of schizophrenia and demographic and socio-environmental characteristics. The second study is a Factor analysis of OPCCI

items from a total of 421 schizophrenia patients in Riyadh who presented between 2009 and 2011, while the third study a descriptive DUP (duration of untreated psychosis) study which focused on describing the duration of untreated psychosis in and to identify any association between the DUP and both patients demographic factors and their first pathway to care.

The results showed that the incidence rate of schizophrenia in Saudi Arabia is similar to those recorded in Western countries with an associations between schizophrenia incidence and younger age, male gender, single status and unemployment. Lack of association between population density and area level income with schizophrenia incidence was also confirmed. The second study produced five-symptom dimensions, mania, depression, reality distortion, disorganisation, and manic /bizarre delusions explaining 33% of the total variance. Different dimensions were differentially associated with the demographic /premorbid risk factors. Results of the third study showed that the median DUP was 1.41 years. Older age at onset, single marital status and higher educational levels were associated with shorter DUP. Long DUP was associated with help seeking from traditional healers.

This thesis has presented a comprehensive picture of the epidemiology of schizophrenia in the capital city of Saudi Arabia, duration of untreated psychosis and a factor analysis of symptoms of schizophrenia.

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LIST OF ABBREVIATION

OPCRIT	The operational criteria checklist for psychotic and affective illness
CDSI	Central Department of Statistics & Information
DUP	Duration of untreated psychosis
ADA	Arriyadh Development Authority
MOH	Ministry of Health
MODA	Ministry of Defence and Aviation
MOI	Ministry of the Interior
KAMC	King Abdulaziz Medical City
KSMC	King Saud Medical City
PSMMC	Prince Sultan Military Medical City
SFHP	Security Forces Hospital Program
KFSH&RC	King Faisal Specialist Hospital & Research Centre
KKUH	King Khalid University Hospital

CHAPTER 1: RESEARCH OVERVIEW

1.1 INTRODUCTION

This thesis reports a research study carried out specifically for a Ph.D. by the author. Three separate analyses were conducted, and these are presented as three papers. The research was conducted first in Riyadh, Saudi Arabia. It involved identifying all first onset schizophrenia cases using health records and collecting clinical and socio-demographic data. Population data was collected to calculate incidence and test for associations with demographic and socio-environmental characteristics. The first study provides knowledge about the epidemiology of schizophrenia by investigating the incidence in Riyadh (Saudi Arabia) and using the incidence data to describe heterogeneity across districts in Riyadh. In addition, the study will test whether variation in incidence occurs according to nationality, sex, age, marital status, employment status, and income. The second study evaluates the five-factor model in Saudi schizophrenia patients by factor analysis of OPCRIT items as rated from the health records. It will also test whether there is any association between the five factors and demographic data included in OPCRIT. The third study describes the duration of untreated psychosis in the capital city of Saudi Arabia to identify any association between both patient demographic factors and their first pathway to care with their duration of untreated psychosis (DUP). Chapter 1, states the overall objectives of the thesis

and each study objectives as well as the research significance. At the end of the chapter a summary of the thesis structure will also be provided.

1.2 OBJECTIVES

The overall aim of the research carried out for this Ph.D., is to describe and achieve a broader and clearer understanding of the epidemiology, etiology and symptomatology of schizophrenia in Saudi Arabia. This will then contribute to the understanding of the psychopathological processes that lead to schizophrenia. The following questions will be considered:

1.2.1 STUDY I - The epidemiological study will address the following:

- Does the rate of schizophrenia differ between Riyadh districts?
- Does the incidence of schizophrenia increase with increasing population density?
- Is the incidence of schizophrenia predicted by the individual and area level variables: migration, younger age, male gender, single status, lower social class and unemployment?

1.2.2 STUDY II- The Factor Analysis of OPCRIT study addresses the following questions:

- What is the OPCRIT dimensional structure for Saudi schizophrenia patients?
- Is there a correlation between social and demographic data included in OPCRIT (sex / age / family history (psychosis / schizophrenia) / use of drugs /alcohol / social status / premorbid personality disorder/ psychosocial stressor prior to onset) with factors scores on the OPCRIT?

The answers to these questions will highlight the symptom pattern of schizophrenia in Saudi patients, and it will allow comparison of the results with Western studies that might lead to a better understanding of schizophrenia symptoms.

1.2.3 STUDY III- The DUP study addresses the following issues:

The Duration of Untreated Psychosis among Saudi patients with schizophrenia will be described and the following questions addressed:

- Is there a significant association between DUP and age, gender, marital status, education level, employment, socioeconomic status, substance misuse and pathway to care?

By answering the above, this part of the thesis will give an indication as to how long it takes a psychotic patient to seek help from a medical provider. It will also provide a clearer understanding of the causes of a long DUP and its association with demographic variables in Saudi Arabia.

1.3 RESEARCH SIGNIFICANCE

The findings of the research are expected to be significant in several ways:

- An important contribution to the schizophrenia epidemiology literature with regard to distribution, aetiology and symptomatology in Saudi Arabia.
- The study provides an essential foundation for future studies such as measuring the effect of social change.

- The findings will be useful for planning new strategies for mental health care services.
- The results of this study will help promote the needs for plans to educate people with schizophrenia and, therefore, encourage them to seek medical help needed.
- The results of this study might help to intensify medical services in the areas most in need of mental health services.

1.4 THESIS STRUCTURE

This thesis focuses on the epidemiology, etiology and symptomatology of schizophrenia in Saudi Arabia. The research findings are presented as three separate papers following a background discussion of the context, a literature review and a description of the research methodology. The thesis structure is formulated as following:

Chapter 1: This chapter will provide an essential overview of the thesis. It contains the research aim, questions and study significance. The structure of the thesis will also be provided in this chapter.

Chapter 2: This chapter describes the background context for the whole thesis. It will provide information about both Saudi Arabia and schizophrenia. Firstly, detailed information will be provided about Saudi Arabia in general and specifically about Riyadh, the capital. The mental health care system will also be covered in this chapter. This chapter will discuss attitudes towards schizophrenia that include cultural beliefs, stigma and service use. Secondly, this chapter

provides basic information about schizophrenia, such as definition, diagnosis and its history, especially in Arab countries.

Chapter 3: This chapter will present the literature review for the whole thesis, divided into three sections. The first section overviews previous studies of schizophrenia epidemiology in both Western and Arab societies in terms of incidence, prevalence and distribution of the disease, it also highlights socio-environmental risk factors. The second section focuses on previous literature regarding the analysis of OPCRIT items to generate factors and dimensions of schizophrenia, mostly in western communities due to lack of Arabic studies on this topic. Finally, the last section discusses previous studies on duration of untreated psychosis and its relationship with demographic factors and the first pathway to care.

Chapter 4: This chapter describes the research methodology in general, including the choice of study design, ethical approval, hospitals included in the study, case ascertainment, data collection, data management and strategy of analysis. It also provides details of OPCRIT and explains why it was used for this study.

Chapter 5: This chapter presents the first paper "Epidemiology of schizophrenia in Riyadh, Saudi Arabia". Describing the epidemiology of schizophrenia in Riyadh (Saudi Arabia) and using incidence data to demonstrate heterogeneity across districts in Riyadh. In addition, this study tests whether variation occurs according to nationality, sex, age, marital status, employment status, income and population density. This chapter is presented in a paper format, arranged into introduction, methods, results and discussion.

Chapter 6: The second paper will be presented in this chapter, "Factor Analysis of Schizophrenia symptoms, signs and demography in a Saudi Sample". It evaluates the five-factor model and tests for associations between the five factors and socio-demographic data included in OPCRIT. An introduction, methods, results and discussion related to the topic will be presented in this chapter.

Chapter 7: The third paper, "Duration of untreated psychosis and pathway to care in Riyadh, Saudi Arabia" will be presented in this chapter. A description of the duration of untreated psychosis in Riyadh and its association with both patient demographic factors and their first pathway to care will be provided in this chapter. The paper includes introduction, methods, results and discussion.

Chapter 8: This chapter provides the final discussion and conclusion for the whole thesis. The results will be briefly summarised, and the limitations of the research discussed. Finally, recommendations and suggestions for Saudi Arabia mental health services, mental health education and future research will be made.

1.5 SUMMARY

A brief introduction to this thesis was provided in this chapter. It has outlined the objectives and the significance of the study as well as the structure of the thesis. The following chapter will be a background chapter for the whole thesis. It will provide information about schizophrenia and the Saudi context.

CHAPTER 2: BACKGROUND

2.1 INTRODUCTION

As described earlier, the aim of this study is to describe the epidemiology, aetiology and symptomatology of schizophrenia in Riyadh, Saudi Arabia. This chapter is a background for the whole thesis. Firstly, it will describe the Saudi context, by providing comprehensive information on topics related to this study and it's arranged into three main parts. The first part covers Saudi Arabia demography in general. The second part highlights Riyadh demography specifically and the history of mental health services. The last part will discuss attitudes towards schizophrenia that include cultural beliefs, traditional healers, stigma and service use. Finally, chapter 2 will also provide information about schizophrenia, such as conceptualisation, definition, diagnosis and its history especially in Arab countries.

2.2 THE SAUDI CONTEXT

2.2.1 Saudi Arabia: Location, People, Culture, Religion and Language

Saudi Arabia is an oil-rich Arab country located in the Middle East. Riyadh is the capital. According to the last census in 2013 by the CDSI (Central Department of Statistics & Information) the population in the kingdom was **29,994,272** (**20,271,058** Saudi). The Saudi Arabia population growth rate until 2013 was 2.7%.

Most Saudis are ethnically Arab; however a small number are from mixed ethnic origin. There are also a significant numbers of residents from Asia mostly from

India, Pakistan, Afghanistan, Bangladesh, Indonesia, and the Philippines (Al-Rabdi, 2004). The country has a conservative Muslim culture, around 98 to 99% are Sunni and 1 to 2 % are Shia. The family is the most vital social foundation in Saudi Arabia, and it is considered to be the primary base for life. Saudis take their family responsibilities seriously. The extended family system and family social support are the norm (Al-Subaie & Al-Hamad, 2000). Arabic is the main language in Saudi Arabia, but the English language is used widely in business, and it is also a compulsory subject taught in schools.

2.2.2 Riyadh Background

2.2.2.1 Riyadh Demographic Profile

The word 'Riyadh' means 'garden' in the Arabic language. It is the capital of Saudi Arabia, located in the Nejd district, the central region of the Kingdom. Over the last fifty years, Riyadh has transformed from a small city to a contemporary city. Riyadh covers around (2000) square kilometers. The city of Riyadh has one of the highest population growth rates globally according to the General Census of Population and Housing results (CDSI, 2013). The total population of Riyadh is 5.7 million inhabitants, and the annual growth rate is 4%.

Riyadh is arranged into 15 municipal districts in addition to the Diplomatic Quarter. Each district is divided into several neighbourhoods (150 in total). Riyadh districts are under the control of Riyadh Municipality and the Riyadh Development Authority (ADA). See appendix 1 for more information about Riyadh districts and neighbourhoods.

Figure 2.1: Riyadh Neighbourhoods Map


الهيئة العليا
لتطوير مدينة الرياض
منطقة الملك عبد العزيز الحربية
العيينة والجبيلة
الغيروان
العارض
النرجس
بنبان
الرمال
مطار الملك خالد الدولي
الجنادرية
الرمال
الياسمين
الملقا
الربيع
النفل
الغدير
حطين
الروح
النخيل
المرسى
جامعة الملك سعود
الملك عبد العزيز
الدرعية
الهدا
الديرة
المربع
الوزارات
الربوة
الورود
الحمراء
المهدية
الوشام
الشهداء
الحزم
الفوارة
بدر
عكاظ
ديراب
الحمد
عريض
الحائر
المنصورية
المصفاة
هيت
المدينة الصناعية الجديدة
طيبة
الإسكان
الدفاع
المناخ
السلي
النور
الفيصلية
الجزيرة
الفيحاء
السعادة
الروابي
خشم العان
النسيم الشرقي
الرمايه
النهضة
الخليج
العزيزية
الصناعية
الشهداء
الدار البيضاء
الصناعية
المنصورية
الصناعية
النظيم
الفاخرية
المونسية
الشفا
العزيزية
الغدير
الورود
النهضة
الربوة
الربوة
الربو

In Riyadh, Saudi citizens constituted 61% of the total population, compared to 39% for foreigners. There is a difference in gender among the Saudi population and non-Saudis. For the Saudis, there are similarities between the proportion of males and females, with the percentage of males 52% (1,808,004) versus 48% for females (1,668,096). In contrast, there is a significant disparity between the number of males (1,533,008) and females (689,013) for the population of non-Saudis in Riyadh, where the ratio of females is about one-third the number of males (male 69 %, female 31%). This is due to the non-Saudi population coming to work in Riyadh (CDSI, 2010). Table 2.1 shows Riyadh urban indicators for the year 2013.

According to ADA (2013), the overwhelming majority of the Saudi population is young. The proportion of those under 15 has decreased by 35%, however, the median age for Riyadh citizens is 22 years old (18 years for Saudi citizens and 30 for non-Saudis).

According to the ADA (2013), there have been significant increases in the amount of families that live in Riyadh. There are two types of families, the individual family comprising of parents and children, and the extended family consisting of spouses and relatives. The pattern of Saudi families has changed since 1986 and has become more of the individual type (75% in 2004) rather than the extended type (21% in 2004). However, both types share a common Saudi family structure. Members of individual families consider themselves part of their original extended family, so they share a physical and emotional bond with them; this means very few Saudi families can be considered nuclear in the strict sense of the term (Al-Subaie & Alhamad, 2000). The normal family size in the Riyadh is 6.2 members. The average

Saudi family has 7 members while the average of non-Saudis family has 4.7 members (ADA, 2013).

Regarding the level of education, the latest statistics (ADA, 2011) show the percentage of enrolment in educational levels for the Saudis from primary level to university level (between the ages of 6 to 30) is 92% (i.e. 92% are educated at or above primary school level), which indicates a significant improvement compared with the rate recorded in 1996 of 88%.

The number of the workforce in Riyadh had increased during the past years reaching 1.3 million people (41% of Saudis and 59% of non-Saudis). The reason for the low percentage of Saudis is due to the large number who are studying (39%) and the large proportion of housewives (21%). However, the unemployment rate in Riyadh for the year 2011 was 12% (ADA, 2011).

The latest statistics show that the total combined amount of yearly income for the Saudis is 26 billion Saudi Riyal (1 Riyal = 3.75 U.S. dollar). The highest income groups live in the western and norteastern parts of the city. The middle income and below average income groups live in the central parts of the city that is the east, south, and southeast of the city (ADA, 2011).

Table 2.1 Al-Riyadh Urban Indicators for the year 2013

Indicator	Value	Indicator	Value
Population	**5.7**	**Population Growth Rate**	**4%**
Proportion of Saudi population	**61%**	**Proportion of Saudi male**	**52%**
Proportion of non-Saudi population	**39%**	**Proportion of Saudi female**	**48%**
Proportion of Saudi age group 0-14	**35%**	**Proportion of non-Saudi male**	**69%**
Proportion of Saudi age group 15-59	**60%**	**Proportion of non Saudi female**	**31%**
Proportion of Saudi age group <60	**5%**	**Number of families**	**919.000**
Av. No of Family Members	**6.3**	**Population Density**	**224person/ha**
Education Enrolment (6-22 years)	**92%**	**Illiteracy Rate**	**8%**

(ADA, 2013)

2.2.2.2 Riyadh health services

The Ministry of Health (MOH) is the main government organization that provides health care for residence of Saudi Arabia. The budget of Ministry of Health in 2009 was 29,518,700 (SR) (110,695,125 USD), which constituted 6.2% of the total government budget of 475,000,000 SR (178,125,000 USD) (MOH, 2009).

Health services, including medication, are provided free in MOH hospitals. There are other independent government sectors that provide and finance health care services in the KSA such as the National Guard, the Ministry of Defence and Aviation (MODA), the Ministry of the Interior (MOI) University hospitals in addition to specialist hospitals. Although in these hospitals treatment is free, admitting patients requires special permission (MOH, 2009). The government (including both the MOH and other government sectors) is the largest health care provider, operating 68.7% of the hospitals, providing 78.9% of the available beds, and employing 77.5% of the medical staff (MOH, 2009). Health services are provided through private health facilities including hospitals, clinics laboratories, and pharmacies throughout Saudi Arabia (MOH, 2009).

In 2009, the total number of hospitals in Saudi Arabia was 393 (75 in Riyadh region). Of the 75 hospitals 49 (65.3%) are governmental hospitals, and 26 (34.6%) are private (MOH, 2009). In Riyadh city there are 13 MOH and governmental hospitals (with a capacity of 8856 beds) and 26 private hospitals (with a capacity of 5281 beds) (ADA, 2013).

2.2.2.2 Mental health services

Before 1970 in Saudi Arabia, psychiatric services were given the lowest priority, as there was little awareness of mental illness, and an acute shortage of psychiatrists; therefore, the vast majority of people had no access to psychiatric treatment.

In 1962, the first mental hospital in Saudi Arabia was established in Taif (Shhar Hospital) serving up to 1800 patients in 1978. Most of the staff were from other Arab countries. They helped to train the native staff and workers. It has gradually become a centre for postgraduate studies and psychiatric nursing training (MOH, 1984, 1988). 1983 was the beginning for a new stage in the mental healthcare system in Saudi Arabia with the establishment of smaller sized (20-120 beds) hospitals and outpatient clinics around the country (Al-Habeeb & Qureshi 2010). These outpatients' mental health clinics treat 1.846 users per 100.000 populations per year. 50% of patients are female, and they are more likely to use mental health care services than males, 36% of these outpatients are diagnosed with Schizophrenia (Qureshi et al., 2013).

Today psychiatry and social health care in Saudi Arabia are provided by a number of psychiatric and general hospitals and clinics (MOH, 2009). Beside the Taif Hospital (570 beds), there are 14 independent mental hospitals all over the country; each has an average bed capacity of 30 to120 beds. There are 61 psychiatric clinics within general MOH hospitals with 20 to 30 beds each. In addition, other governmental health sectors, such as the National Guard and university hospitals provide 165 beds for psychiatric inpatients. There are also a great amount of private clinics and

outpatient clinics in general private hospitals providing psychiatric care (MOH, 2009).

Unlike developed countries, there are almost no community mental health care (CMHC) services for mental health patients, which explain why patients with chronic mental illnesses are resident in mental hospitals (AL-Habbeb & Qureshi, 2010). Mental health services in primary care are still very limited. Trained GPs treat only minor mental disorders while referring more severe cases to the secondary level (AL-Habbeb & Qureshi, 2010).

In Riyadh, there is The Amal Complex for Mental Health, which is a specialist (MOH) mental hospital with the capacity of 428 beds. Beside the psychiatric hospitals, a high proportion of general hospitals have established psychiatric wards, including King Saud Medical City (KSMC), King Abdulaziz Medical City (KAMC), Prince Sultan Military Medical City (PSMMC), Security Forces Hospital Program (SFHP), King Faisal Specialist Hospital & Research Centre (KFSH&RC), King Khalid University Hospital (KKUH).

2.2.3 Attitudes Towards Schizophrenia In Saudi Arabia

2.2.3.1 Cultural Beliefs

Culture is defined as "a socially shared, trans-generationally communicated, system of implicit values, beliefs and attitudes, and explicit behavioural codes of practice" (Kroeber & Kluckhohn, 1952). Culture, therefore, can be shaped by religion, race, level of education, economic status, and political factors (Al-Shahri, 2002). Saudi Arabian culture like any other Arab Gulf country is considered to be a traditional culture. In these cultures interdependence is encouraged rather than independence (El-Islam, 2008).

Saudi society tends to explain the sudden disturbed behaviour that appears in a person to be the result of witchcraft, evil eye and demonic possession rather than scientifically explained as 'mental illness'. Jinn (demons), Sihr (magic) and Al-Ein or Nafs (evil eye) are all mentioned in the Holy Qur'an and that explains why they are mostly accepted in society (Al-Krenawi et al, 2000; Al-Subaie & Alhamad, 2000; Okasha, 2005). As a result of this belief, the recognition of mental illness can be delayed which affects the disease progress and treatment(El-Islam, 2008).

'Demonic Possession' can be explained in two ways. One is that the person had harmed the jinni by accident, such as spilling something hot around sunset, and the jinni takes revenge by possessing the patient. The second explanation is that the jinn falls in love with him or her (Al-Shawi, 1998). The Holy Qur'an Says,

"Those who consume interest cannot stand [on the Day of Resurrection] except as one stands who is being beaten by Satan into insanity…" (**Al-Baqarah , 275)**

'Al-Ein' or 'Nafs' which mean 'evil eye' is based on an Islamic principle. A person with an evil eye is believed to have the power to harm others with negative spiritual powers (Koenig, 2009) causing them physical illnesses, injuries, or emotional disturbance (Al-Subaie &Alhamad, 2000). The Holy Qur'an says,

"Say: I take refuge with the Lord of the dawn. From the evil of what He has created. And from the evil of the dark night when it comes. And from the evil of those who blow on knots (practice Secret Arts). And from the evil of the envious (one) when he envies" (An-Nas)

'Sihr' involves the belief that witchcraft (strictly forbidden in Islam) is responsible for a problem especially in marriage and sexual life (Al-Shawi, 1998; Al-Subaie & Alhamad, 2000; Koenig, 2009). The Holy Qur'an states,

"....Suleiman (Solomon) did not disbelieve, but the devils disbelieved teaching men magic..." (Al-Baqarah, 102)

2.2.3.2 Traditional Healers

Traditional healers, in most Arab countries, provide informal and unofficial health care. However, most of the time, no contradiction occurs between the medical treatment and the traditional healing (Okasha, 2003). It is essential to mention that traditional medicine is a legal major health system in Saudi Arabia. About 50% to 70 % of psychiatric outpatients have sought help from a traditional healer at some point of their illness; 21% to 50% did that before even being seen by a psychiatrist (Hussein, 1989; Al-Subaie, 1990). Traditional healers are usually native religious middle-aged men with no modern medical background. They share the same language, beliefs, and tradition of their patients. No charge is required for their services, but they accept donations. It seems that age, sex, social class, and education

do not have an impact on a patient's choice between traditional healings and modern psychiatry (Al-Subaie & Alhamad, 2000).

Al-Habeeb (2003) conducted a pilot study in the Qassim region in Saudi Arabia to analyse the pattern of psychological symptoms and treatments given by faith healers. The sample consists of 45 faith healers who were given a pre-designed, self-administered, semi-structured questionnaire. Results showed that most healers do not have a clear conceptualisation of psychiatric symptoms. They tend to recommend therapeutic methods derived from the religious concepts to their clients who, they claim, show improvement in their mental state. This study indicates a need to increase societal awareness of the limited capacity of faith healers to reach the correct diagnosis and to use an appropriate remedial method. It also indicates the need to educate society about the important role of psychiatrists and the services they provide that can reduce the stigma of mental illness. This could be one of the causes why many prefer to see faith healers instead of going to psychiatric clinics.

2.2.3.3 Stigma

According to Goffman's definition of stigma, 'It occurs when there is a marked relationship linking the identified person via attributional processes to undesirable characteristics which discredit him or her' (Brohan et al., 2010). People with mental disorders face stigma and discrimination in most societies (Kadri et al., 2004). The mental illness stigma is a major obstacle to recovery and can reduce employment opportunities and social functioning for patients and their families (Struening et al., 2001). This was shown in several studies performed in developed countries (Jorm et

al., 1999; Crisp et al., 2000). The tendency to stigmatise and discriminate against people with mental disorders is not exclusive to Western countries; it occurs in Asia as well.

Kadri et al. (2004) carried out a study in Morocco to examine family members' attitude towards schizophrenic patients using a structured questionnaire on a sample of 100 family members. Each participant was responsible for a schizophrenic patient. The mean age of the caretakers was 47.4 years, 69% female (50% were mothers), about a third of the women were without an education, and about three-quarters had no job. The patients had a mean age of 30.4 years, were more likely to be male, single, unemployed, with duration of illness ranging from 10 months to 30 years. The results showed that 63% of caretakers did not give the patient difficult tasks; 34% justified this by admitting their distrust towards them and 14% believed that the patient was handicapped. In the study, 14% of family members reported treating the patient with distrust, 8% treated the patient as if they were mad, 15% treated the patient with rejection and aggressiveness. However, 37% said that they treated the patient just like any other family member.

El-Adl & Balhaj (2008) conducted a study in the UAE to evaluate public views of mental illness stigma, and to hear their opinion regarding an organisation that could reduce this stigma. They used a questionnaire, which they developed and circulated to a sample of the public (n=4000). The response rate was 2222 (55.5%), the majority of participants were between 15 and 30 year old, they were from both genders with slightly more females (52.3%) than males (40%). In the study, 1875 (84.4%) believed that the mental illness stigma was a problem caused by society.

The risk of stigma was highest in cases of HIV (73.3%), followed by mental retardation (62%), and mental illness (61.6%). The results showed that individuals suffering from HIV and mental disorder are less likely to receive public support compared to others suffering from blindness, deafness, or physical disability. The study showed that 38% believed that females suffering from mental illness are at higher risk of being stigmatised than males, and 56.9% believed that the family suffers more if the patient is female. This study showed clearly that mental illness stigma is a significant problem in Arab society. A comprehensive programme is essential to fight the stigma, support sufferers, and improve public awareness of mental illness.

Mansour (2008) conducted a cross-sectional school based study in Saudi Arabia to identify and evaluate the beliefs of adolescents about schizophrenia in terms of etiological factors, symptoms, and psychiatric treatment. Three hundred female high school students were randomly chosen to answer a pre-designed questionnaire, which was an adapted form of the questionnaire established by the World Psychiatric Association (WPA) against schizophrenia stigma and discrimination. This study revealed unexpected findings, that is, 83.7% of the sample knew about schizophrenia, more than half of the sample considered it to be a mental disorder, 33.7% saw it as a neuropsychiatric disorder, 27% thought it was split personality disorder, and only 4% considered it as a kind of jinni that affected the diseased person. Television (47.3%) and newspapers (27%) were among important sources of knowledge and information about mental illness in this study. In terms of schizophrenia symptoms, only 22.7% knew that hallucinations and delusions are key features of schizophrenia. This study revealed a negative attitude towards

schizophrenic patients, that is, 32.3% refused to talk to them and 31% refused to accept such patients with them in the class. This result is consistent with Gureje et al., (2005) whose results indicated that most people avoided social interactions like having a conversation with people with mental disorders, and they would be disturbed by working with a person with a mental illness.

2.2.3.4 Service Use

After reviewing the existing studies regarding epidemiology data especially the occurrence and prevalence rates of mental disorders in Saudi Arabia, Al-Subaie & Alhamad (2000) said that they found a number of striking results. First, the amount of males seeking psychiatric help is much higher than the amount of females. Nevertheless, this result may not indicate the true prevalence of mental disorders in the Saudi society for several reasons, including the fact that Saudi women prefer seeking help from traditional healers. Additionally, the total reliance of women on men to take them to hospitals may prevent them from attending hospitals as frequently as men. Another explanation pointed to the role of the extended family in potentially decreasing morbidity among women (El-Islam et al., 1986).

The second finding showed that most of the psychiatric service users are in the second and third decades of their life. This can be explained as they are part of the age group that is struggling between traditional and modern values due to the rapid urbanisations and changes in life-style in this part of the world (Sayed et al., 1986) and that this is the peak age of onset for many psychiatric disorders. The low numbers of old people can be understood in terms of Islamic teachings and cultural

traditions that encourage the showing of respect and care for the elderly (Al-Subaie & Alhamad, 2000).

2.3 SCHIZOPHRENIA

Schizophrenia is a serious mental disease, which affects approximately 1% of people worldwide (Minzenberg et al., 2008). The disorder has a variety of symptoms that involve cognition, feelings, perception and different parts of behaviour that impair the patient's ability to function and socialise normally (Buchanan & Carpenter, 2005). Schizophrenia patients commonly experience auditory hallucinations and are prone to delusions of conspiracy or disguised acts of harm against them. The severity of symptoms in schizophrenia may vary greatly. Only the mildest cases of schizophrenia do not affect aspects of everyday life, while the moderate to more severe cases of the disorder may prevent patients from maintaining jobs, personal relationships, or even caring for themselves (Keefe & Harvey, 1994).

2.3.1 Diagnostic Criteria

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (APA, 1994), and the International Classification of Diseases (ICD-10) (WHO, 1992), are both major current descriptive classifications were the most widely used clinical instruments when I started this thesis. The two classifications are shown in the figures below.

Figure 2.2 : DSM-IV Diagnostic Criteria for Schizophrenia

A- Characteristic symptoms: Two or more of the following, each present for a significant portion of time during a one-month period:

- Delusions
- Hallucinations
- Disorganized speech (e.g., frequent derailment or incoherence)
- Grossly disorganized or catatonic behavior
- Negative symptoms (i.e. affective flattening, alogia, or a volition). Note Only one of Criterion A symptom is required if delusions are - bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

B - Social/occupational dysfunction: Since the onset of the disturbance, one or more major areas of functioning, such as work, interpersonal relations, or self-care are markedly below the level previously achieved.

C- Duration: Continuous signs of the disturbance persist for at least six months. This six-month period must include at least one month of symptoms (or less if successfully treated) that meet Criterion A.

D- Exclusion of schizoaffective disorder and mood disorder with psychotic features.

E- Substance/general medical condition exclusion: the disturbance is not due to the direct physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition.

F- Relationship to a pervasive developmental disorder: If there is a history of autistic disorder or another pervasive developmental disorder, the diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated

Figure 2.3: ICD-10 Diagnostic Criteria for Schizophrenia

Either at least one of the syndromes, symptoms and signs listed below under (1), or at least two of the symptoms and signs listed under (2) should be present for most of the time during an episode of psychotic illness lasting for at least one month (or at some time during most of the days).

1. At least one of the following:

   - Thought echo, thought insertion or withdrawal, or thought broadcasting.
   - Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception.
   - Hallucinatory voices giving a running commentary on the patient's behavior, or discussing him among themselves, or other types of hallucinatory voices coming from some part of the body.
   - Persistent delusions of other kinds that are culturally inappropriate and completely impossible (e.g. being able to control the weather, or being in communication with aliens from another world).

2. Or at least two of the following:

   - Persistent hallucinations in any modality, when occurring every day for at least one month, when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas.
   - Neologisms, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech.
   - Catatonic behavior, such as excitement, posturing or waxy flexibility, negativism, mutism and stupor.
   - "Negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (it must be clear that these are not due to depression or to neuroleptic medication).

2.3.2 Schizophrenia Symptoms

The disorder can be considered to be comprised of three major groups of symptoms: positive symptoms, negative symptoms, and cognitive symptoms (Mueser et al., 1997). The division into positive and negative symptoms evolved from the influence these symptoms have in diagnosis and treatment (Crow, 1985; Andreasen et al., 1995). Positive symptoms are things 'added', or they are noted by their presence (Kavanagh, 1992), and they appear to reflect an excess and abnormal function (Peralta & Cuesta, 1998). Other research findings suggested subdividing the positive symptoms into two dimensions: psychotic and disorganization due to the different outcomes, psychological correlates, and structural brain abnormalities for each type (Andreasen et al., 1995).

2.3.2.1 Positive symptoms

A. Delusions

Possibly one of the best delusion definitions is Jaspers's (1913) that proposed three criteria; "first, it is a belief held with extraordinary convictions, with an incomparable subjective certainty, secondly, there is imperviousness to other experiences and to compelling counterargument, and thirdly, the content is imposable" (cited in Hirsch & Weinberger, 1995). A belief that is not built in reality is incorrigible to argument (McKenna, 2007). These are the most common schizophrenic symptoms (Hirsch & Weinberger, 1995).

Common schizophrenic delusions include:

i. ***Delusions of persecution*** - The patient believes that others are following him/ her, or that he/she is being treated unfairly by others (McKenna, 2007).

ii. ***Delusions of reference*** - An unrelated event in the world is believed to have a special and personal meaning. For example, articles in newspapers or the words in a song are about them (McKenna, 2007).

iii. ***Delusions of grandeur*** - The belief that one is much greater and more powerful than he really is (McKenna, 2007).

iv. ***Delusions of control*** - The false belief that one's ideas, actions, or feelings are caused by another person, or are under alien control (Mishara et al., 2009).

B. Hallucinations

They are known as "apparent perception of an external object when no such object is present" (Hinsie & Campbell, 1970). According to Cutting (1990), the most common hallucination is auditory (50%), followed by visual (15%) and tactile hallucinations (5%).

C. Disorganized speech/thinking

Disorganized speech is one of the key characteristics of schizophrenia, such as blocking of thoughts, unrelated answers to questions and speaking incoherently (Andreasen & Black, 2000).

D. Disorder of behaviour

This includes grossly disorganized behaviour and catatonic behaviour that causes severe problems in a person's ability to meet day-to-day activities, e.g., bathing, dressing properly, and even eating regularly (Pull, 2002). Guggenheim and Babigian (1974) reported that catatonic (unusual postures and motor responses) symptoms appear in 5% of all new diagnosis of schizophrenia.

2.3.2.2 Negative Symptoms

Negative symptoms represent the absence or lack of mental function that should normally be present in a healthy person (Kavanagh, 1992). For instance, people with schizophrenia frequently seem emotionless, flat, and apathetic. These symptoms are associated with poorer prognosis (Moscarelly et al., 1996).

Negative symptoms include:

- Lack of motivation in life and activities including relationships and sex.
- Blunted affect which means that the person appears to lack any emotion at all (found in 50 % of acute or chronic patients).
- An inappropriate affect (found in 20% acute patients) (Andreasen, 1979).
- Inexpressive faces and the voice may sound monotonous.
- Few spontaneous movements and not wanting to leave the house.
- Poverty of speech such as short answers that do not carry much meaning.

2.3.2.3Cognitive Symptoms

Cognitive symptoms of schizophrenia refer to the way a person thinks. Although these are not considered diagnostic criteria for schizophrenia, some are fairly common with the illness. They include:

- Inability to sustain focused attention (Kremen et al., 1994).
- Difficulties in solving problems and making decisions that prevent them from planning and structuring activities (Goldberg et al., 1995).

- Memory problems, as schizophrenia often effects working memory and the ability to store and manage information immediately after learning it (Saykin et al., 1991).
- Lack of insight and an unrealistic understanding that prevents them from realizing that they are ill.

2.3.3 Cross-cultural differences in symptoms

Many researchers indicated that the incidence, symptoms, course, and outcome of schizophrenia might vary from culture to culture. Schizophrenia positive and negative symptoms may vary from culture to culture (Myers, 2011). A study conducted by Bauer et al. (2011) on (n = 1080) schizophrenic patients in seven countries (Austria, Georgia, Ghana, Lithuania, Nigeria, Pakistan and Poland) was undertaken to comprehend the impact of different cultures on the type of hallucinations in schizophrenia that appear in these different societies.

Findings showed that patients from West Africa had the highest rates of auditory (Ghana: 90.8%, and Nigeria: 85.4%), and visual hallucination (Ghana: 53.9%, and Nigeria: 50.8%), while the lowest rates of auditory hallucination were identified in Austria (66.9%). The lowest rates of visual hallucinations were found in Pakistan (3.9%). With regard to negative symptoms, an American and Sweden cross-national studies was conducted to compare the performance between schizophrenic patients in these two countries in terms of daily functioning, disabilities facing them in real world, and achievement of goals. Results demonstrated that because of the way of obtaining and maintaining housing in Sweden does not require a high mental capacity, the Swedish sample lived more independently and for longer periods of time than New York (Harvey et al., 2009).

2.3.4 The Outcome of Schizophrenia

Many outcome studies suggest that there are variations in outcomes seen in individuals with schizophrenia. Much of the reason for this is unknown, but there is evidence that different factors are involved, including demographic factors like socio-economic status, premorbid personality traits, biological factors, and illness. Management factors are also involved, including the duration of illness before treatment and medication (Rosen & Garety, 2005).

One of the factors that predict the outcome is the familial morbid risk. Many studies state that a family history of affective psychosis is linked with a good outcome in schizophrenia (Anglin et al., 2009). Fowler et al. (1972) and Kendler & Tsuang (1988) examined this argument. Fowler et al. (1972) divided schizophrenic patients and their relatives into two groups where 28 showed a good-outcome and 25 showed a poor-outcome. They found that first-degree relatives of the poor-outcome group have a 10% risk of developing schizophrenia, but this risk decreased to 4% in the good-outcome group. The risk of developing affective disorder was lower in the poor-prognosis group, but this result was not statistically significant. Kendler & Tsuang (1988) studied 253 schizophrenic patients and their 723 first-degree relatives. Findings indicated that the morbidity risk for affective disorder was significantly higher for relatives of the good-outcome group while the morbidity risk for non-affective illness was higher among family members of poor-outcome patients (not significant).

One of the most main risk factors for poor outcome and a less favourable course is premorbid dysfunction (Bromet et al., 1974). This was reported in several studies

that examined 163 schizophrenic patients to determine the premorbid social functioning impact on schizophrenia outcome (Bailer et al., 1996). The results indicate that impaired premorbid social functioning is associated with impaired social course of schizophrenia.

Many studies suggested that lower childhood IQ and poorer cognitive functioning are associated with an unfavourable outcome (Aylward et al., 1984). Aylward et al. (1984), found through their review and meta-analysis of research on IQ and schizophrenia that childhood, adolescence, and early adulthood IQ scores in pre-schizophrenic were lower compared to their peers with similar social class origins.

Many follow up studies have shown that women have a better outcome than men (Bardenstein et al., 1990). The key outcome in this study is that long-term outcomes are more favourable for women than for men in terms of social and work functioning, time symptomatic, drug abuse, and marital and parental status. In addition, further evidence suggests that an earlier age (before the age 18) of onset of psychosis is associated with poor course and prognosis in schizophrenia. For example, the study of Nimgaonkar et al. (1988) that was carried out on 53 inpatients diagnosed with schizophrenia - with or without a genetic predisposition to this disorder - showed that early age of onset is linked with a poor response to antipsychotic drug treatment. Table 2.2 summarizes the strongest predictors of outcome.

The idea that schizophrenia had more favourable course and prognosis in developing nations rather than developed countries emerged mostly from three

cross-national studies by the World Health Organization (WHO). The first is the 'International Pilot Study of Schizophrenia' (IPSS) (WHO, 1979), the second is the 'Determinants of Outcome of Severe Mental Disorder' (DOSMeD) (Jablensky et al., 1992), and the third is the 'International Study of Schizophrenia' (ISoS) (Harrison, et al., 2001). However, a review of 23 studies in 11 low-medium income countries (Brazil, Bulgaria, China, Colombia, Ethiopia, India, Indonesia, Jamaica, Nigeria, South Africa, and Trinidad) questioned the validity of this idea and called for a re-test (Cohen et al., 2008). The disorder outcome and course had varied significantly. Some studies in India strongly supported the 'better outcome' hypothesis (Thara, 2004), while Brazil (Menezes et al., 1997) and China (Ran et al., 2001) had contradictory findings.

Good patterns of recovery and social functioning were found in India (Thara, 2004) and Indonesia (Kurihara et al., 2005) but were poorer in Nigeria (Gureie et al., 1999). Gender had an impact on social functioning. Women in India (Thara, 2004) and those in rural China (Ran et al., 2001) had a better course and outcome. On the contrary, men had a better outcome in Colombia (Hopper et al., 2007). Nigeria was the opposite as continuous psychosis occurred more frequently among women and they were also more likely to relapse (Ohaeri, 1993).

Table 2.2: Summary of the strong predictors of outcome

Factor	Good Outcome	Poor Outcome
Demographic	Female	Male
	Married	Single
Genetic	Family history of affective disorder	Family history of schizophrenia
Onset	Good premorbid adjustment	Schizoid traits
	Acute onset	Slow onset
	Life event at onset	Long duration of untreated psychosis
	Early treatment	
Symptoms	Affective symptoms	Negative symptoms
		Obsessions
Psychosocial	Good response to treatment	High expressed emotions
		Substance misuse

(Lewis & Buchanan, 2005)

2.3.5 Brief History Of Schizophrenia

***Before 1800*.** The history and the existence of schizophrenia before the modern era, especially prior to the eighteen-century is controversial. Many consider schizophrenia to be recorded since the age of antiquity, "that it can be traced in the written documents to the old pharaonic Egypt as far back as the second millennium before Christ" (Kyziridis, 2005). Half a million cuneiform tablets were written in 3200 B.C. in ancient Iraq, several thousand of them were covered with medical texts (Abdul-Hamid, 2003). Kinner Wilson, a British archaeologist, studied and analysed a number of tablets that contained information about psychiatric disorders (Wilson, 1996). He found that these texts described epilepsy and a number of mental illness associated with it like phobias, obsessive-compulsion, and persecutory delusions. There was a description of a patient with severe psychotic symptoms that may fit the diagnosed symptoms of the disease of schizophrenia in accordance with Schneider's symptoms (Abdul-Hamid, 2003). However, in the pre-classical and classical times

these signs were thought to be the consequence of supernatural forces invading the patent as a punishment for immoral behaviour (Abdul-Hamid, 2003; Lewis & Buchanan, 2005). It was also noted that in ancient India and Rome they recognised conditions similar to schizophrenia disorder (Jeste et al., 1985). However, there was a shift in understanding of mental illness back then towards a naturalistic standpoint (Howells, 1991). Moving towards medieval times, especially in Western societies, there was a return to a pre-classical explanation of mental illnesses by Arabic physicians who kept the classical models of illnesses alive by practicing medicine according to Hippocratic, Aristotelian, and Galen ideas (Lewis & Buchanan, 2005). "Schizophrenia has probably existed as long as mankind", said Strongren (1982). Kraepelin (1913) noted 'this disease is probably extremely old' (p.232). Lewis thought 'that some such disorder has probably always been recognised' (Hare, 1988).

On the other hand, Hare (1988) considered schizophrenia a recent disease; he pointed out several pieces of evidence that supported the argument against the existence of schizophrenia before 1800. A recent study by Evans et al. (2003) analysed the old Greek and Roman texts looking for a description of schizophrenia. Results demonstrated that there was no proof of the modern diagnostic criteria of schizophrenia in this literature. Dendle (2005) reviewed hundreds of demon possession cases from the early medieval times and discovered little evidence of a condition similar to schizophrenia.

Another hypothesis says that schizophrenia is a recent disease and suggested a link between this disease and industrialisation. Cooper and Sartorius (1977) clarified this hypothesis with three key points. First, industrialisation led to improvements in

health and medical care that led to a decrease in the mortality rates during infancy and childhood. This meant that vulnerable children who would previously have died young now survived. If they later developed schizophrenia, there was an increased risk of chronicity. Second, during industrialisation the size and structure of towns and communities grew to the degree that it became difficult to accommodate schizophrenic patients in these societies. They faced rejection from their communities and tended to be put in special institutions. The third key point was that the psychological and social structure of families was influenced by the progress of industrialisation, and this had an impact on their schizophrenic members.

It is important to differentiate psychosis, which has many causes, and schizophrenia, which is a particular form of psychosis. It seems likely that irrespective of whether it existed in the pre-industrialised era, the incidence and prevalence seems to have increased.

Schizophrenia in the Islamic world The nation of Islam began around the seventh century when the entire Middle East was occupied by Muslims. Mental illness existed in the Islamic empire. This is proven by key pieces information: first, famous Muslim physicians of medieval periods, such as "Ar –Razi", "Ibn Sina", "Ishaq Ibn Imran", and "Al-Majus Ibn Sina" pointed out the term 'insanity' in their work (Youssef et al, 1996). Islamic medicine was influenced by Galen's medical system (the humoral theory). This can be obviously seen in the work of Al-Razi who was the first Islamic physician to discuss neuropsychiatric diseases from 841-926 A.D. (Al-Issa, 2000). Al-Razi said that mental diseases were not due to evil spirits but rather due to a nervous breakdown or psychic disorder (Al-Subaie & Alhamad, 2000). He wrote a 24-volume medical encyclopaedia *kitab al-Hawi,* which contained a whole

chapter on melancholia and other mental illness (Al-Issa, 2000; Pridmore & Pasha, 2004). Another medical book written by "Ibn Rabban at-Tabari" in the ninth century A.D. contained a whole chapter on brain diseases (Kyziridis, 2005). Ibn Sina wrote the 14-volume cannon of medicine, which was used in the West for 700 years (Pridmore & Pasha, 2004). "Al-Majusi, Ishaq ibn Imran" (d. 982) discussed mental illness in his book *Kitab al-Malaki* and mentioned some common symptoms of melancholia such as fear, sadness, delusions, and hallucinations (Al-Issa, 2000). The second key is the existence of psychiatric hospitals; they were called *bimaristan* (a place for the sick in Persian). In the early stages of the ninth century the first Islamic hospital was established in Baghdad and was supported by the Caliph Harun Al-Rashid (d. 809) (Al-Issa, 2000.). This was followed by a number of others in many major cities like Cairo where the hospital was funded in 872-873 A.D. by Ahmad ibn Tulun. Basra and Syria followed with similar hospitals (Youssef et al., 1996; Dols, 1987, 1992). However, the existence of psychiatric hospitals in Arab culture, which is encouraged by Islamic principles to take care of the mentally ill at home, indicates that these hospitals contained serious cases of psychosis probably similar to schizophrenia, although the term schizophrenia itself did not exist (Youssef, 1996). This tendency to keep most patients at home emphasises the role of the family and its responsibility towards ill members (Al-Issa, 2000).

It is clear by reading the history of Islamic psychiatry that depression, melancholia, and other sorts of mental illness were discussed in the works of Muslim physicians. However, the concept of psychosis itself was not formulated even though hallucinations and delusions were reported as symptoms of mental illness (Al-Issa, 2000).

Schizophrenia in the 19th century In the early 19th century, both John Haslam (1764-1844) and Philippe Pinel (1745-1836) described mentally ill individuals - who are recognized nowadays as schizophrenic patients - according to the contemporary nosology (Hales et al., 2008, p. 408). However, our understanding of schizophrenia developed when Emil Kraepelin, a German psychiatrist, identified its symptoms in the late 19th century (Andreasen, 1997). He used the term Dementia Praecox. The word 'dementia' means a gradual decline in mental functions while praecox means premature (Moscarelly et al., 1996; Pull, 2002). He distinguished this disease, which he found affected adolescents, from other kinds of dementia that were more common late in life (Moscarelly et al., 1996; Weinberger & Harrison, 2011). Kraeplin recognised that a small number of 'dementia praecox's patients recovered completely even though he believed that a chronic disorder had led to the deterioration of the personality (Herz & Marder, 2002). Most European psychiatrists followed Kraeplin's narrow view of schizophrenia (North & Yutzy, 2009). The term "schizophrenia" was initially presented by Swiss psychiatric Eugene Bleuler early in the 20th century to replace Kraeplin's term of dementia praecox. The term "schizophrenia" comes from two Greek roots meaning 'split mind' and is used to describe the disintegration of mental function that can happen in people with this disorder (Weinberger & Harrison, 2011). Bleuler (1950) had a broader approach to schizophrenia as he realised that he might be dealing with group of disorders. However, the narrower approach to schizophrenia was accepted by most psychiatrists around the world (Riecher- Rössler & Rössler, 1998).

Neither Kraepelin nor Bleuler used the terms 'positive symptoms' and 'negative symptoms'. It was Hughlings Jackson who applied these terms to determine the

primary from secondary neurological phenomena (Weinberger & Harrison, 2011; Pull, 2002).

Both Karl Jasper and Kurt Schneider depended on form rather than content when approaching the definition of schizophrenia (Weinberger & Harrison, 2011). Schneider's work was considered an important perspective in the development of the concept of schizophrenia. He reviewed many case records and divided the schizophrenia symptoms into two groups, first-rank symptoms and second-rank symptom (Pull, 2002).

The problem faced by psychiatrists, psychologists, and researchers was the lack of agreement on diagnostic criteria for mental illness, which caused a decrease in the degree of confidence and reliance on available diagnostic criteria (Spitzer et al., 1978).

In 1970, the original version of 'Feighner criteria' was developed. The criteria were dedicated to the diagnosis of 15 mental illnesses. Later, there were some changes in the criteria, and new groups were added. This new set of criteria was known as the Research Diagnostic Criteria (RDC) and showed much greater reliability than the previous version (Spitzer et al., 1978; Pull, 2002).

The identification and definition of the schizophrenia criteria in the RDC relied on Schneider's first-rank symptoms in order to exclude borderline and paranoid states.

2.3.6 Prevalence of schizophrenia in Saudi Arabia

It ought to be noted that the literature about schizophrenia incidence in Saudi Arabia is very rare even though the Ministry of Health in Saudi Arabia (2008) had reported that 22% of mental health patients have psychosis, However, there are few published papers focusing on issues associated with schizophrenia rather than the epidemiology of schizophrenia in Saudi Arabia such as Zarroug (1975), Chaleby & Tuma(1987) and Kent & Wahass(1996).

2.4 CONCLUSION

Essential information about Saudi Arabia especially about healthcare services was provided in this chapter. This chapter highlighted the significant role played by both culture and religion in the perception and treatment of mental disorders in Saudi Arabia, which explains why Saudis prefer seeking help from traditional healers rather than professional services. It also has provided background information about schizophrenia. The following chapter will provide a literature review for this study.

CHAPTER 3: LITERATURE REVIEW

3.1 INTRODUCTION

This section of the thesis provides an overview of the numerous studies that have been conducted into this topic and is thus categorized into three key themes. The first theme is about schizophrenia epidemiology. The second theme is about schizophrenia symptom factor analyses. The third theme is about duration of untreated psychosis (DUP)

3.2 THEME ONE: EPIDEMIOLOGY OF SCHIZOPHRENIA

3.2.1 Introduction

Epidemiology is "the study of distribution and determinants of diseases" (MacMahon & Pugh, 1970). Therefore, Psychiatric epidemiology involves identifying the quantity of individuals receiving psychiatric care in the area, those that are considered at an elevated risk of suffering from mental health issues, and the reasons for them being categorized as such. Epidemiological studies are important in understanding the etiology of diseases (Tandon et al., 2008). One important line of epidemiological research involves examining the impact of the geographical place in the distribution of psychotic illnesses. One contemporary study illustrates that regional variances exist in terms of the amount of individuals suffering from schizophrenia, as well as variances between those residing in large cities and between the two genders (McGrath, 2004).

Most of the research done into schizophrenia has been done on people living in developed countries, which mean that it symbolizes only a small part of the global population. A wide range of lifestyles and exposure to environmental factors, in addition to the genetic variation among populations in developing countries, can add important information to our knowledge about the etiology of schizophrenia. Therefore, epidemiological studies of schizophrenia need to be expanded to developing countries. These studies would serve not only the needs of people in developing countries, but also advance our overall knowledge of schizophrenia etiology.

There is a serious shortage of epidemiological studies of schizophrenia in Saudi Arabia with few publication addressing schizophrenia-related aspects. Nevertheless, the rapid socio-economic and cultural changes that the Saudi society has had to deal with over the last few decades seems to have had an impact on increasing the number of psychiatric patients (Al-Subaie, 1990). The Ministry of Health in Saudi Arabia released a study in 2008 that showed that over one-fifth of all mental health patients (excluding inpatients) were suffering schizophrenia-based difficulties with their behavior and mental health. Generally, studies on the incidence of schizophrenia in Saudi Arabia have focused mostly on specific issues associated with the disease without attempting to investigate the countrywide demographics of schizophrenia (Zarroug, 1975; Chaleby & Tuma, 1987; Kent & Wahass, 1996).

The first part of this chapter provides information about the epidemiology of schizophrenia. At first, it talks about schizophrenia incidence and prevalence in developed and developing countries before it mentions the socio-demographic and

environmental risk factors associated with schizophrenia such as age and gender. Finally, it focuses on the spatial variation in incidence of schizophrenia and highlights the neighborhood factors, which may have an impact on the distribution of psychotic illnesses.

3.2.2 Schizophrenia incidence and prevalence

3.2.2.1 Schizophrenia Incidence

Incidence rates are one of the main indicators of morbidity. Incidence refers to 'the number of people from a specified population who developed a new case of a disorder during a specific time period' (Moscarelly et al., 1996). As Eaton (1999) and Jablensky (1999) pointed out, schizophrenia epidemiology was initially largely concerned with the idea that schizophrenia has a similar incidence across cultures and geographical areas.

Indeed, this argument is supported by Jablensky et al. (1992) and Sartorius et al. (1986), who investigated various areas in numerous countries: Ibadan in Nigeria, Cali in Columbia, Prague in Czechoslovakia, Nagasaki in Japan, Moscow in the Soviet Union, Nottingham in England, Rochester and Honolulu in the USA, Dublin in Ireland, Agra and both rural and urban Chandigarh in India, and Aarhus in Denmark. This study seemed to demonstrate that incidence rates of schizophrenia across cultures are similar and that patients in the developing world have a better outcome compared to those who live in developed countries.

The idea that there was no variation in incidence was increasingly challenged by the findings of many other studies. Recent systematic reviews, for example, have indicated that schizophrenia rates vary significantly across different population, areas, and groups (McGrath et al., 2004; Cantor-Graae & Selten, 2005). Around a decade ago, the field of schizophrenia epidemiology was greatly impacted by the work of one group of scholars who took a total of 55 research studies (representing 33 nations) as case studies, and found that a median average of 15.2 schizophrenic episodes were recorded for every 100,000 individuals. Furthermore, the 80% of values in the middle exhibited a variance five times the size (McGrath et al., 2004). They also pointed out gender differences by asserting that schizophrenia tends to occur more often among men than women, with around 1.4 men to every 1 woman.

Rates in urban sites tended to be higher than mixed urban-rural sites. In terms of migrants versus native-born individuals, migrant groups had an increased rate of schizophrenia. Cantor-Graae & Selten (2005) questioned if migrants had an increased risk for schizophrenia. They collected findings from previous studies regarding this issue that were published between 1977 and 2003. The results showed that migration played a major role in developing schizophrenia.

In the Arab world, there are very few epidemiological studies. Even these few studies had focused on issues associated with schizophrenia rather than the epidemiology of schizophrenia. However, one study was conducted in Benghazi, Libya by Avasthi et al. in 1991. The aim was to analyze the socio-demographic and diagnostic factors of psychiatric in-patients by analyzing their medical records. Half of these patients were new cases, and the others were readmission cases; 89% were

native Libyans, 8% were foreign Arabs, and 3% were non-Arab foreigners. This distribution was identical to the original distribution of the general population. The majority of participants from Libya were men (62%) aged 15-34 (66%). Of these men, over one- third were married (37%), over one-quarter were unemployed (28%), and some were working for the army (16%). Using ICD-9, schizophrenia was found to be the most common disorder (39%).

It may be essential to draw attention to some points regarding the results of socio-demographic characteristics of the Libyan patients. The findings showed a high number of males in the in-patient population (62%). In an attempt to clarify the small number of mentally ill in-patient females in Arab countries, Sayed et al. (1986) suggested that one reason for that might be women's dependency on men to bring them to the hospital. Furthermore, that society tended to consider their symptoms as part of feminine behavior and not in need of medical intervention. This explanation must be taken with caution due to the nature of schizophrenia; that is, the person does not have enough awareness and insight to go to the hospital to ask for a treatment by himself/herself. As a result, a member of the family must take such a decision. This study showed a higher proportion of male inpatients possibly reflecting greater severity amongst males. This study also contradicts a number of other studies that confirm that the proportion of psychiatric morbidity among immigrants is higher than among the indigenous population. However, it was not diagnosis specific (Rwegellera, 1977; Hitch & Rack, 1980). Basher (1973), Bazzoui & Al-Issa (1966), and Chowdhury (1966) conducted studies in which an in-patient percentage of higher than 39% was found in other developing countries' mental health institutions.

Another study was conducted to evaluate the incidences of schizophrenia based on first hospital admission in Bahrain. In this study, 200 men and 125 women began treatment for schizophrenia between 1988 and 1996. The findings show that each year, out of 10,000 people in Bahrain, there were an average of 1.29 schizophrenic episodes reported. Furthermore, when narrowing this population down to those aged 15-54, an average of 2.13 schizophrenic episodes were experienced each year (Abdul Karim & Al Haddad, 1998).

3.2.2.2 Schizophrenia Prevalence

Prevalence means the "number of people with a disorder during a defined period of time" (period prevalence) or "at a specific point in time" (point prevalence) (Moscarelly et al., 1996). Prevalence studies of schizophrenia published between 1965 and 2002 were identified and reviewed by Saha et al. (2005). Prevalence rates based on core migrant and other special groups showed that the median rate for point prevalence[1] was 4.6/1000 and 3.3/1000 for period prevalence[2]. It was 4.0 for lifetime prevalence[3] and 7.2 for lifetime morbid risk[4]. There was no statistically significant difference between cities, rural areas, rural-urban areas, or genders. However, high prevalence rates of schizophrenia occurred among migrant groups while the lower rates were found in developing countries.

On the other hand, schizophrenia epidemiological studies that were published between 1980 and 2000 were systematically reviewed in order to analyze the

[1] Point prevalence: the number of individuals exhibiting an illness at a specific moment, on a specific day, or during a specific month, etc.

[2] Period prevalence: the number of people exhibiting an illness over a certain duration, such as a year.

[3] Lifetime prevalence: the number of people who have exhibited an illness at any point (excluding those deceased at the time of an investigation).

[4] Lifetime morbid risk: the likelihood that an individual will exhibit the illness between certain points during their lifetime, or by the time they reach a particular age.

heterogeneity in incidence and prevalence rates for schizophrenia. Significant variations were found in 1-year and lifetime prevalence of schizophrenia. Schizophrenia rates showed variation by up to 5 fold. These findings supported the hypothesis that schizophrenia incidence and prevalence rates vary significantly around the world (Goldner et al., 2002).

Few studies were carried out in the United Arab Emirates regarding the rates of psychiatric disorders. However, one research project, which focused on the ratio between the number people who had experienced at least one schizophrenic episode in their lifetime (and other relevant illnesses) and the number who had not, combined with the psychiatric morbidity of the general population, was carried out on a sample of 1394 adults chosen systematically from the Al Ain community. In the group, 49.1% were females, most respondents were aged between 18 and 40, and 68.3% were married. This study used a number of tools, "the Composite International Diagnostic Interview (CIDI)" version 1.1, "the new screening psychiatric instrument", "the Self-Reporting Questionnaire (SRQ-20)", and "the Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID) screening module". The study showed a total lifetime prevalence rate of 8.2 % for ICD-10 psychiatric disorders with a female to male ratio of 2:3 while the total lifetime prevalence rate was 0.7% for ICD-10 schizophrenia and related disorders. The authors said that the reduction in this number compared to the West might be due to reasons that include mental illness stigma especially for men in the Arab societies. In addition, this survey did not include individuals in institutions or mentally impaired people (Abou-Saleh et al., 2001).

Another cross-sectional community psychiatric survey was conducted in Dubai, UAE (Ghubash et al., 1992). A sample of 300 women was chosen randomly to evaluate the rates of mental illness among UAE women in Dubai. Every participant involved in the research was questioned using the following three tools: Brown and Harris' (1978) Life Events and Difficulties Schedule; Ghubash et al.'s (1992) Sociocultural Change Questionnaire; and Wing et al.'s (1974) PSE (9th Edition). Results showed a high prevalence in that 22.7% of women in Dubai had minor psychiatric disorders (13.7% depressive disorders; 7% anxiety). Schizophrenia was found in only one case (0.3%). It was found that psychiatric disorders were the most prevalent in women who had lost their husbands to death, women who had gone through divorce and separation, women who were married polygamously, and women raising children on their own. As such, it can be seen that schizophrenia seems to be linked to marital status.

A retrospective descriptive population based study was conducted in Doha (Qatar) to assess the occurrence of acute and transient psychotic disorders and to determine its socio-demographic characteristics. In this study, all Qataris, non-Qatari Arabs, and foreigners whether in-patients or outpatients (n = 724, 125; nationals constituting about 30% of the general population) were included for the period of seven years. Data were gathered from patients' medical records and with the use of ICD-10 the results showed that 174 patients were diagnosed with psychotic disorders (69% males and 31% females). The most common was acute schizophrenia-like psychotic disorder (35.6%). In terms of gender, social status, and nationality, no significant differences in the frequency of acute and transient psychotic disorders were reported (Shaltout et al., 2007).

3.2.2.3 Risk Factors

A risk factor is "an attribute/exposure which is associated with an increased probability of schizophrenia, but not necessarily causal" (Murray, 2002). According to Cooper (1987) these factors can be grouped into three categories: demographic factors (age, gender, social class, ethnicity), predisposing factors (family/genetic background, season of birth, obstetrical complications, prenatal infections, substance abuse), and precipitating factors (life events, stress). With regard to risk factors for developing schizophrenia, a family history of the disorder is still the strongest (Züchner et al., 2007). Having a parent with schizophrenia increases the risk to 10%. Scientists like Kendler & Diehl (1993) focused on the genetic basis of schizophrenia. These scholars argued that schizophrenic etiology should be largely concerned with hereditary influences. McGuffin et al. (1994) noted that the evidence for a genetic contribution to schizophrenia is compelling. However, more recent research has shown that genetic and environmental factors may be interconnected, that is, individuals with an inherited tendency towards schizophrenia may develop this disorder if it is triggered by an environmental factor (Picker, 2005).

Mortensen et al. (1999) conducted their research in Denmark where they examined the ways in which schizophrenia could be caused by environmental factors. A total of 2,669 schizophrenic episodes were recorded for 1.75 million people. These people all had mothers who were born between 1935 and 1978 in Denmark. When focusing on the potential of hereditary influence, it was discovered that there was a 9.31% increase in the likelihood of experiencing a schizophrenic episode when an individual's family had also suffered from the illness as opposed to individuals whose family members had never had a schizophrenic episode. Furthermore, it was

found that individuals were more likely to experience schizophrenia when they were born in large cities. The season of the year also had an influence on the likelihood of experiencing the illness. It was discovered that for individuals with family members who had suffered from schizophrenia, there was a 5.5% population attributable fraction (PAF). The season in which the individual was born was linked to a PAF of 10.5%. It seems that the largest PAF (34.6%) was being born in a large city.

Many studies have questioned the association between the prevalence of early childhood trauma among adults and psychotic disorders (Morgan & Fisher, 2007). One study suggested that individuals who had experienced extreme upset and poor upbringings as children may be more likely to become schizophrenic and psychotic as adults. Hallucinations and other psychosis symptoms are strongly related to childhood abuse and neglect (Read et al., 2005).

- **Age and Gender**

Schizophrenia affects both sexes; it appears early in the lives of both sexes with about the same frequency. However, schizophrenia appears earlier in men than in women. Schizophrenic male patients are more likely than female patients to have poor premorbid adjustment, with more frequent and more severe relapses and abnormalities in brain structure. In contrast, women diagnosed with schizophrenia are more likely to experience late-onset psychosis (Michael et al., 1996, p. 277).

Many studies have supported the claim that the disorder may appear slightly earlier in males than in females (Lewine, 1981; Häfner et al., 1993). One group of researchers analyzed the information of almost 200 individuals suffering from

schizophrenia (or schizoaffective disorders) to investigate the influence of gender and age on late-onset (female) and early-onset (male) patients. It was found that males who developed the illness at an earlier age (and women who developed the illness at a later age) exhibited worse performance than males who developed the illness at a later age (and women who developed the illness earlier in life) (Lewine et al., 1981). Thus, most studies found that onset age differs significantly between males and females. Men are more likely to report their first onset in their early 20s compared with the mid-to-late 20s for women (Lewine, 1981; Loranger, 1984; Goldstein et al., 1989; Shtasel et al., 1992; Szymanski et al., 1995).

Goldstein et al. (1989) tested the hypothesis that schizophrenic patients experience different subtypes of the disorder according to their gender. The sample consisted of 332 schizophrenic patients. Survival analysis was used to estimate the age of onset. Findings suggested that men tend to experience a more severe form of schizophrenia.

In the Loranger (1984) study, 200 schizophrenic patients (100 for each gender) were examined. Findings suggested that men experienced their first psychotic episode approximately five years earlier than women. About 90% of male patients compared with 66% of female patients, developed schizophrenia before the age of 30. On the other hand, 17% of women and 2% of men developed schizophrenia after the age of 35. 10% of women presented psychotic symptoms for the first time after the age 40.

In the Shtasel et al. (1992) study, a sample of 107 schizophrenic patients – off medication - (Male: 74 and female: 33) were rated by measures of symptom type and severity. Results showed that, in terms of negative symptoms, men were more severely impaired than women while no significant differences were reported regarding positive symptoms. Results also indicated that women were socially functioning more effectively than men.

One study focused on the variances between men and women who had experienced their first schizophrenic episode in terms of four different factors: biologic, onset, reaction to treatment, and course of treatment (Szymanski et al., 1995). The researchers found that female patients exhibited more progress than male patients when given medication for the illness. Furthermore, it was found that women developed schizophrenia at a later stage than men did. In addition, some studies suggest that women during their mid-to-late 40s suffer from a second peak. (Flor-Henry, 1990; Häfner et al., 1994).

Although previous epidemiological studies noted that both sexes experienced schizophrenia with equal frequency (Dohrenwend & Dohrenwend, 1976; Lewine, Burbach, & Meltzer, 1984), newer research suggests that incidence rates are higher among males than among females (Iacono & Beiser, 1992). Aleman et al. (2003) reported that the males had a higher risk of developing schizophrenia than the female in their meta –analysis study which consists of 38 studies. Compared with women, men have more hospitalizations and longer hospital stays (Goldstein et al., 1989; Test et al., 1990). One group of researchers suggest that women's experience of schizophrenia is more benign than men's; that it develops later in life; and that

women's behavior and performance is greater than men's prior to the exhibition of schizophrenic symptoms (Castle et al., 1995).

Another study investigated the information of 374 individuals suffering from schizophrenia, with a specific focus on the influence of gender on the prevalence of specific types of schizophrenia (Beratis et al., 1997). In terms of paranoid subtype, no significant differences were reported between the two genders. However, the residual and the catatonic subtypes appeared to be more common among males than females.

A study was conducted in Saudi Arabia to analyze the clinical and socio-demographic characteristics of admitted patients over a 10-year period starting from 1988. The sample consisted of 1366 patients (683 of each sex) and had 2217 admissions in 10 years (19.5% had schizophrenia) (AbuMadini & Rahim, 2002). The findings showed that most schizophrenic patients were males, although mood and anxiety disorders were more prevalent in females. This finding was supported by Shaltout et al. (2007) results. They noted that out of 174 individuals who were diagnosed with an acute and transient psychotic disorder over a seven-year period, 69% were males. The Al Ain Community Psychiatric Survey showed no gender differences at all (0.7% for women, 0.7% for men) (Abou-Saleh et al., 2001).

3.2.3 Spatial Variation in Incidence of Schizophrenia

One of the main approaches in epidemiology involves highlighting the spatial and geographical variations in the distribution of psychotic illness (March et al, 2008).

Some research was carried out primarily in developed nations with an emphasis on the ways in which the etiology of psychosis might have been influenced by social environmental variables (March et al., 2008). The link between urbanicity and the increased incidence of schizophrenia has been confirmed in several studies, especially for persons who already have a familial risk for the disorder (Lewine et al., 1997; Pedersen & Mortensen, 2001; Arehart -Treichel, 2003).

Early attempts to address the geographical distribution of psychosis may go back to Faris and Dunham in Chicago in 1939, who discovered that schizophrenia was highly prevalent in downtown urban areas in which housing standards were poor and social links were weak. In contrast, the lowest incidence rates were found in the outskirts of the city consisting of high standard residential areas. Their findings encouraged more research into the association between the social environment and the risk of schizophrenia. In modern times, positive correlations have been found between individuals living in heavy urban areas and the occurrence of schizophrenia, according to research (primarily cohort) conducted in Europe and the United Kingdom.

It has also been discovered that the likelihood of developing schizophrenia is 50% lower in rural regions than it is in cities, according to two scholars who meta-analyzed a series of studies on developed nations (Krabbendam & Van Os, 2005). This result cannot be explained by bias even though the reason for this association is not clear yet. Another study showed that an increased risk of developing schizophrenia is associated with the number of years lived in a higher level of urbanization. According to Pedersen and Mortensen (2001), individuals who resided

in the largest cities before the age of 16 were 2.75 times more likely to suffer from schizophrenia.

It is suggested that the likelihood of suffering from schizophrenia increases with urbanicity due to a number of elements typically associated with large cities. It was demonstrated that schizophrenia was most highly influenced by being born in a city and other family members having suffered from mental illnesses or schizophrenia, based on the investigation of data from 2.66 million Danish citizens. In Ireland, a prospective study of psychosis and urbanicity showed that males tend to develop schizophrenia more than females in urban compared to rural sites. Incidence rate ratio (IRR) was 1.92 for men and 1.34 for women (Kelly et al., 2010).

A systematic review of studies investigating the incidence of psychosis according to urbanicity and neighborhoods was conducted by March et al. (2008). A total of 44 studies, all from developed countries, (20 of urbanicity and 24 of the neighborhood) were included in the review. Urbanicity studies indicated that urban areas have twice the rates of the rural areas. These findings were consistent with Krabbendam & Van Os (2005) findings. Several studies pointed to the timing of exposure to urbanization. Danish, Dutch, and Swedish research has shown that individuals are at greater risk of developing psychotic illnesses when they are born in heavy urban areas. Furthermore, it has been found that the likelihood of suffering from a psychotic experience increased with the duration of childhood spent residing in cities. This being said, Marcelis et al. (1998) found that Dutch individuals who were not born in cities yet spent time residing in cities at an older age were no more likely to suffer from psychotic episodes, unlike individuals born in cities. Furthermore, individuals born in cities were found to have a higher likelihood of suffering from

psychosis even if they did not live in a city when their psychosis began to develop. One researcher has suggested that it is likely that these results are accurate and that drift hypothesis is not responsible for the higher risk of mental illness in this case (March et al., 2008).

Most of the neighborhoods studies (20 from European countries, 4 from US) showed heterogeneity of incidence rates between districts, electoral wards, or other small area units. Among the most intriguing findings in the neighborhood studies are those testing ethnic density and psychosis. There is no neighborhood research specifically focusing on the ways in which psychosis is affected by the length of experience with this variable.

Overall, the research seems to show that neighborhood types, and urbanicity have varying effects on the likelihood of an individual experiencing a schizophrenic episode. Based on the link between the higher prevalence of psychotic illness and residing in a city, it appears that environmental influences that appear during childhood have a high impact on the likelihood that an individual will suffer from schizophrenia at some point. Conversely, it appears that it is largely social elements that are linked to neighborhood factors when it comes to the prevalence of schizophrenia.

3.2.3.1 Variation by Neighborhood

Tracts, municipalities, electoral wards, districts, and so on, are the terms most frequently used to determine one neighborhood from another. A number of neighborhood studies focused on the neighborhood composition; immigration and

ethnicity, including ethnic density and ethnic fragmentation (Schwartz & Mintz, 1963; Klee et al. 1967; Rabkin, 1979; Boydell et al, 2001; Shaw et al., 2012). Some researchers, such as Kirkbride (2008), Van Os et al. (2000), and Jaco (1954), have concentrated on the potential link between the distribution of psychotic patients/incidences and the social connections within neighborhoods, as well as the number of residents living within certain neighborhoods, but researchers are currently unsure as to whether or not the likelihood of an individual suffering from psychosis is linked to the density of the population in a given area.

Psychosis and schizophrenia have also been studied in terms of numerous alternative neighborhoods factors such as socio-economic deprivation (Faris & Dunham 1939; Hare, 1956a/b; Hollingshead & Redlich, 1954; Dauncey et al, 1993; Allardyce et al., 2005; Lofors & Sundquist, 2007; Kirkbride, 2008). Overall, a huge portion of available research papers has stated that there is a variance between the numbers of psychotic episodes between the neighborhoods of developed nations. Unfortunately, to the best of the researcher's knowledge, no neighborhood studies have been conducted in any of the Arab countries.

I. Ethnic Density and Ethnic Fragmentation

The hypothesis of "ethnic density" suggests that individuals of ethnic minority groups have a higher risk of developing psychosis if they live in areas with lower proportions of people of the same ethnicity (Shaw et al., 2012). Old ecological studies which were conducted in US showed an association between ethnic density and mental disorders. An example of such studies includes the one conducted by Schwartz & Mintz (1963) on Italian Americans in Boston, Massachusetts. The

researchers discovered that Italian American schizophrenic patients were less frequently found in residential areas with heavy Italian American occupancy.

One Baltimore study investigated the link between the number of admissions to mental health institutions and the white to non-white ratio among patients. It was discovered that the minority group (i.e. those whose ethnicity was represented by less than one tenth of the population) had the most admissions (Klee et al., 1967). The findings of this study are in line with another research paper, which investigated the link between the likelihood of mental hospital admission for New York City's Puerto Rican, white, and black populations and ethnic density (Rabkin, 1979). The rates were higher among the smallest ethnic group compared to the other residents in the same area.

More recent studies have showed mixed results. One research study conducted in the United Kingdom supported the findings of American studies by illustrating that the lower the density of non-white ethnic minority groups in London, the higher the prevalence of schizophrenia for those ethnic groups (Boydell et al., 2001). On the other hand, one study investigated the relationship between schizophrenic hospitalization and the densities of various ethnic groups (Caribbean, Pakistani, Indian, and Irish). It was discovered that Irish males were more likely to be hospitalized for schizophrenia in neighborhoods where the density of the Irish ethnicity was high. However, there was no evidence to suggest that hospitalization was more likely for individuals of other ethnic groups who lived in neighborhoods where their ethnicity was well represented (Cochrane & Bal, 1988). This study used extremely large areas as the units for analysis possibly obscuring an ethnic density effect.

II. Role of Socio-economic Status

The highest rates of schizophrenia are found among the lower socio-economic classes. Socio-economic deprivation was mostly examined in many studies. One influential research project conducted during the 1930s in Chicago investigated the prevalence of schizophrenia around numerous neighborhoods within the city. The researchers found that poorer, lower-class neighborhoods experienced higher rates of schizophrenia, with 102.3 occurrences per 100,000 people (age 15-64 years old) and it decreases when moving towards higher-status peripheral areas (Faris & Dunham, 1939). . This distribution has been confirmed in other cities including Bristol, UK (Hare, 1956-a) and Mannheim, Germany (Häfner & Reimann, 1970). Faris & Dunham (1939) suggested that unsatisfactory living conditions caused schizophrenia. A search for isolation would be consistent with the finding that people with schizophrenia in disadvantaged areas usually live alone without their families (Hare, 1956-b).

One early study in the U.S.A. found that the incidence and the prevalence of schizophrenia were highest in the lowest socio-economic groups (Hollingshead & Redlich, 1954). One group of researchers carried out a study in Nottingham, England, which focused on the distribution of schizophrenic episodes among city-dwellers. This was achieved through an analysis of longitudinal data from 67 people suffering from schizophrenia; concentrating specifically on their regional movements across their lifetimes. The researchers discovered that the most socioeconomically poor neighborhoods exhibited higher occurrences of the illness than more affluent neighborhoods, with a threefold difference (Dauncey et al., 1993).

The findings showed that incidences of schizophrenia are significantly associated with levels of social and urban deprivation. Furthermore, schizophrenia rates and the economic state of certain neighborhoods were shown to have a linear correlation in two modern research studies carried out by Allardyce et al. (2005) (in Scotland) and Lofors and Sundquist (2007) (in Sweden). The only study that did not uncover a link between poor neighborhoods and the incidence of schizophrenia was an analysis of Dutch data performed by Drukker et al. (2006). Clark (1948, 1949) studied the association between schizophrenia rates and occupational levels in Chicago and found out that the lowest status occupations are associated with the highest rate of this disorder.

One group of researchers found that neighborhoods suffering from greater poverty, households with working-class fathers, and poor parental education were the three key influencers of schizophrenia (Werner et al., 2007). However, another study questioned the relationship between psychiatric disorders and socio-economic status. It was suggested that individuals who were high-risk due to hereditary influences, who had also experienced downward social mobility, were more at risk of suffering from psychiatric illness. Furthermore, social anxiety and conflict was also identified as a key influence. The results indicated that schizophrenia may be a consequence of social selection (Dohrenwend et al., 1992). According to the ECA studies based in the U.S., the risk of schizophrenia in people in the lowest socio-economic quartile was eight times higher than in individuals in the highest quartile (Thornhill, 2011). However, several studies in India have found that the highest rates occur in the upper class rather than in lower class (Rao, 1966). Varma &

Coworkers (1980) noted a similar high frequency of schizophrenia in higher socio-economic groups in an Indian clinic.

In 2006, Kirkbride questioned if the low socio-economic levels for the black and minority groups (BME) was the reason for the high rates of psychosis among them. This study was conducted in East London over two years and used population-based design of first-onset psychoses in subjects aged 18 to 64 years. The results showed that even after age, gender, and socio-economic status were controlled for, all of the BME population had high rates of a psychotic disorder. The highest incidence rate ratios (IRRs) were observed for affective and non-affective psychotic illnesses in mixed black and white Caribbean individuals, with an IRR of 7.7, and 'other' white ethnicities, with an IRR of 2.1. For schizophrenia specifically, female Bangladeshis had an IRR of 2.3; black Africans had an IRR of 2.6, and both Pakistanis and black Caribbeans had an IRR of 3.1 each.

III. Social Capital

Social capital is a "term used to describe aspects of social networks, relations, trust, and power as a function of a community usually defined by a geographical entity" (e.g. a city neighborhood) (Whitley & McKenzie, 2005, p. 73). The oldest research in this area was conducted 60 years ago in Texas, in which it was discovered that there was a clear correlation between schizophrenia and a lack of social ties in certain areas of the state (Jaco, 1954). Social capital plays a key role in causing schizophrenia. This hypothesis was examined in 2008 by Kirkbride et al. who used a cross-sectional questionnaire on social capital to (n=16, 459) in 33 neighborhoods of

South London. This questionnaire contained “social cohesion and trust (SC&T)” and “social disorganization (SocD)”.

The research entitled 'Aetiology and Ethnicity in Schizophrenia and Other Psychoses' (AESOP) was utilized to provide information with which to calculate the incidence rates of schizophrenia. It was discovered that areas with the smallest and largest prevalence of 'SC&T' showed the most cases of schizophrenic episodes. Furthermore, these findings held true despite socio-economic conditions, ethnic distribution and density, ethnicity itself, gender, and age. The findings of this study support what was suggested in other studies; the variations in schizophrenia occurrence are due to different neighborhood factors.

Allardyce et al. (2005) noted in their study, which was conducted in Scotland that living in high socially fragmented neighborhoods was linked with high rates of schizophrenia. Silver et al. (2005) tested the neighborhood effects on the distribution of mental illness using data from the “National Institute of Mental Health's Epidemiological Catchment surveys” (n = 11, 686). They found that high rates of schizophrenia, major depression, and substance abuse disorders were significantly associated with neighborhood residential mobility.

In contrast, a multi-level case–control study was performed in Maastricht, Netherlands, to test the influence of neighborhood social capital on increasing the risk of developing schizophrenia by using both of the “Sampson measures of social capital - SC&T and ISC”. The results did not show any link between schizophrenia occurrence and any neighborhood variables including social capital (Drukker et al.,

2006). These findings however need to set in context of another study from the same area that indicated that other neighborhood-level characteristics might contribute 12% of the heterogeneity in the incidence rates of schizophrenia (Van Os et al., 2000). It is likely that the relatively high levels of social cohesion in this area are relevant.

3.3 THEME TWO: SAUDI SCHIZOPHRENIA FACTOR ANALYSIS

3.3.1 Introduction

Schizophrenia is a mental illness that has existed at least across recent centuries and existed across culture, gender and religion. It has distinctive yet varying manifestations, and there have been many attempts over the years to classify the clinical features of this illness in order to better understand its course, etiology and possible treatment measures (Cardno et al., 1996). Traditionally, symptoms have been grouped according to a categorical classification namely the Diagnostic and Statistical manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) and the International Classification of Diseases (ICD-10) (World Health Organization, 1993). These categorical representations are advantageous in that they are familiar and easy to understand, as well as enabling simpler decision-making. The inherent disadvantage of these classification systems is that they are not based on empirical investigations, but are rather a reflection of historical notions and perceptions, although reliability was tested. The validity of such approach was questioned due to the evidence that indicated an overlap between schizophrenia and other psychotic diagnoses in their premorbid risk factors, medical signs and treatments (Allardyce et al. 2007). Therefore, a dimensional approach was introduced at the International conference that was held in July 2006 when APA and its partners announced a dimensional approach in psychiatric diagnostic systems (Regier, 2007). Allardyce et al. (2007) had defined the psychopathological dimensions as "groups of symptoms which occur together more often than would be expected by chance alone" and this can be approached by using exploratory factor

analysis (EFA) p.429. The dimensional system was derived from empirical research and numerous factor analysis investigations. Nevertheless, while the factor system allows for a more accurate portrayal of the patient's unique presenting symptoms, its focus is more descriptive rather than diagnostic (Van Os et al., 2003). Research suggests that the categorical model is not as effective as the mixed categorical and dimensional (or purely dimensional) model (Van OS et al., 1999; Rosenman et al , 2003: Dikeos et al , 2006; Allardyce et al , 2007) Thus, while the dimensional representation provides more information and does not impose categorical boundaries (often forcing the clinician to categorise the patient as 'atypical'), the number of dimensions and their essence remains a matter for future discussion.

3.3.2 Operational Criteria OPCRIT Checklist

For the past twenty years, OPCRIT (Operational Checklist for Psychotic Symptoms) (McGuffin, Farmer and Harvey, 1991) has been used extensively as a tool for characterising forms of mental illness, consisting of a 90-item checklist based on operational criteria for the major psychiatric classification systems. Though it is used for diagnosis, data derived from its application can be used to further classify and characterise patients' symptoms, in other words it can be used to generate dimensional representations of a patient's illness by calculating his scores on clusters of specific symptoms found to occur together. In this manner, OPCRIT has been used in some studies, which aimed to analyse symptoms of psychotic and affective disorders. These studies demonstrated that the most frequently extracted dimensions have been: mania, depression, positive symptoms, disorganization and negative symptoms. (Brittain et al., 2013a).

While alternatives such as the SANS and SAPS (Scales for the Assessment of Negative and Positive Symptoms) (Andreasen, 1984) define each symptom on an ordinal 0-5 scale, OPCRIT defines psychotic symptoms categorically or with a more limited range. In addition, the OPCRIT includes a wider range of psychotic symptoms, mainly positive ones. Consequently, factor analyses have often involved the division of the positive symptoms into finer categories (Cardno et al., 1996).

So far, there is no final agreement of the number of the symptoms dimensions of psychosis, however most studies suggest three or more factors (Liddle 1987; Murphy et al. 1994; Andreasen et al. 1995). Critics of the three-factor model (positive, negative and disorganisation) state that it oversimplifies the presenting symptoms, and fails to provide useful insight as to a patient's prognosis and course of treatment (Mass et al., 2000). Though various studies have found specific associations between abnormal brain structures and the negative scale, as well as behavioural patterns consistent with the disorganised scale, a five factor model has been proposed to better reflect each patient's unique manifestation of the disease (Mclntosh et al., 2001; Peralta & Cuesta, 2001; Van Dael et al., 2006).

3.3.3 Factor analytical studies based on OPCRIT

Table 3.1 shows factors analytical studies based on OPCRIT in psychosis patients. Most of these studies have suggested four or five factors. Cardno et al. (1996) study was conducted on a sample of 102 patients with DSM-III_R schizophrenia. This study suggested a five-factor model, which accounted for 49.3% of the variance. This study indicated that a five-factor model consisting of the following dimensions (paranoid,

negative, disorganization, first rank delusions and first rank hallucination) is better than a three factor model (Positive, negative and disorganization).

Serretti et al. (1996) conducted a study designed to identify the symptom dimensional structure for major psychoses. 1004 inpatients diagnosed with mood disorders and schizophrenia (DSM-III_R) were included in this study. A total of 500 participants provided data for factor analysis. Following this, the other 504 individuals were involved in a confirmatory factor analysis (CFA) in order to assess the goodness of fit. It was discovered that delusion, disorganisation, depression, and excitement were the four key variables responsible for 54.6% of the variance.

Van Os et al (1997) study was conducted on 150 psychosis patients and 548 of their first-degree relatives, and by using 20 items the study revealed seven factors explaining 63 % of the total variance (inappropriate/catatonia; delusions/ hallucinations; mania; insidious onset / blunting; depression; lack of insight; paranoid delusion). In another study consisting of 66 RDC schizophrenia patients, an eight factors model was found which accounted for 71.0% of the variance. The model consisted of following (positive formal thought disorder; first rank delusions; first rank hallucinations; inappropriate affect/bizarre behaviour; negative symptoms; grandiose/bizarre delusions; delusions of influence/persecution; and other hallucinations) (Cardno et al, 1997).

The aim of the Cardno et al. (1999) study was to investigate if the dimensional model has any genetic basis. The sample consists of 109 sibling pairs with schizophrenia and schizoaffective diagnosis and SAPS; SANS and OPCRIT were used for symptom

rating. Dimensions produced from OPCRIT analysis were: positive, negative, disorganization and first rank delusions. None of the factors showed any association with genetic factors. Later on, from the same perspective, Cardno et al. (2001) conducted another study to evaluate the genetic contribution to symptom dimensions. 224 twin pairs with psychosis disorders were included in this study. The study suggested a six-factor model: disorganized, negative, first-rank delusion, paranoid, other hallucination and first-rank hallucination. This study reported that the score on disorganized dimension was significantly related to genetic loading for psychosis.

One research study investigated the connection between the medically significant variables and symptomatic elements of 204 psychosis patients (Mclntosh et al., 2001). A four-factor structure was suggested: manic, depressive, disorganization and reality distortion.

The available research in this area was enhanced by a further study conducted within the last decade since it explained psychosis' dimensional frameworks as well as evaluating their links to medical elements. This study also evaluated how these elements could be described more effectively using dimensions (Dikeos et al., 2006). 191 psychotic patients were included in this study. OPCRIT measures were studied via factor analysis before conducting a regression analysis of the illness' symptoms and diagnostic factors. Negativity, disorganisation, depression, distortion of reality, and mania were chosen as the five key symptoms, though they were less varied in psychotic illnesses other than schizophrenia than they were for schizophrenia itself. It was discovered that mania was the most effective determinant of affective

psychosis versus schizophrenia. Additionally, it was found that high levels of negativity were linked to greater severity in terms of illness course, a slow but highly damaging onset of symptoms, and lower performance prior to symptoms appearing. Diagnosis was not found to be as effective at understanding illness factors as dimensions were. However, diagnosis still managed to provide strong explanations.

Allardyce et al.(2007) conducted a study based on 464 new cases of psychosis assessed with OPCRIT to describe symptom dimension structure and to compare dimensional and categorical classifications in terms of demographic and pre-morbid risk factors. By using the regression analysis five dimensions were produced, manic, disorganisation, depressive, delusional and auditory hallucinations, explaining 58% of the total variance. Different dimensions were differentially associated with the pre-morbid risk factors. Combining dimensional and categorical models was more successful describing association with the causes and correlates of psychosis rather than each model independently. In terms of the association between dimensions and demographic and pre-morbid risk factors, no significant association was found between gender and any of the dimensions. The disorganisation factor was associated with items: single, unemployed, poor premorbid work and social adjustment while the manic factor was significantly associated with family history of other psychiatric disorders. On the other hand, it had an inverse relationship with being single, unemployed, poor premorbid work and social adjustment. The delusional dimension has an inverse relationship with poor premorbid social adjustment. The depressive dimension was significantly associated with drug /alcohol use, presence of psychosocial stressors and family history of other psychiatric disorders.

In summary and demonstrated by the table below there has been remarkable concordance in factors identified, mania, disorganization, reality distortion (or hallucinations) appearing in almost all suggesting specific psychopathological or neuropsychiatric underpinnings. It remains to be seen however if the same dimensions are relevant in the radically different social and cultural context of Saudi Arabia, taking into consideration, that most of these studies were based on psychosis samples while our study will focus only on schizophrenia sample.

Table 3.1 OPCRIT-oriented examples of research using factor analysis

Authors and year of study	N	OPECRIT items	Diagnoses methods	Number of factors	Names of factors
Cardno et al. 1996	102	26	DSM-III-R[1]	5	Paranoid Negative Disorganization First-rank delusions Hallucination
Serretti et al. 1996	1004(500+504)	38	DSM-III-R	4	Excitement Depression Disorganization Delusion
Cardno et al. 1997	66	19	RDC[2]	8	Positive formal thought First-rank delusion Hallucination Inappropriate affect /bizarre behaviour Negative Grandiose/ bizarre delusions Delusions of influence/persecution Other hallucinations
Van Os et al. 1997	150+ 548 first-degree relatives	20	RDC	7	Inappropriate/catatonia Delusions/ hallucination Mania Insidious/ blunting Depression Lack of insight Paranoid delusion
Cardno et al. 1999	191	26	DSM-IV[3]	4	Positive Disorganization Negative First-rank delusions
Van Os et al. 1999	706	46	RDC DSM-III-R ICD-10[4]	5	Manic Depressive Negative Positive Disorganized symptoms

[1] Diagnostic and Statistical Manual of Mental Disorders, Third Edition - Revised (American Psychiatric Association 1987)

[2] Research Diagnostic Criteria (Spitzer et al. 1978)

[3] Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (American Psychiatric Association 1994)

[4] International Statistical Classification of Diseases and Related Health Problems, Tenth Edition, Diagnostic Criteria for Research. Geneva: World Health Organization 1993)

Cardno et al. 2001	224	18	RDC	6	Disorganized Negative First-rank delusion Paranoid Other hallucination First-rank hallucination
Mclntosh et al. 2001	204	39	ICD-9[5]	4	Manic Depressive Disorganization Reality distortion
Serretti et al. 2001	2241	46	DSM-IV	4	Excitement Delusions Depression Disorganization (negative)
Murray et al. 2005	387	62	ICD-9 ICD-10	4	Depression Reality distortion Mania Disorganization
Dikeos et al. 2006	191	51	RDC DSM-IV	5	Mania Reality distortion Depression Disorganisation Negative
Allardyce et al, 2007	464	28	DSM-IV ICD-10	5	Manic Disorganisation Depressive Delusional Auditory hallucination

[5] International Classification of Diseases, Injuries and Causes of Death, Ninth Edition (World Health Organization 1977)

3.4 THEME THREE: DURATION OF UNTREATED PSYCHOSIS (DUP)

3.4.1 Introduction

In medicine, accurate early diagnosis leads to efficient treatment and often reduces the anxiety due to removal of uncertainty. It also decreases the disability, which might have been caused while waiting for the correct diagnosis and treatment.

The benefits of early intervention and treatment in any illness are generally acknowledged; therefore early diagnosis of the illness is necessary to obtain treatment at the earliest point possible. However, psychiatry is known for its diagnostic delay for a several reasons. One reason for this is the lack of biological correlates of some psychiatric disorders. On the other hand, fear of stigma and rejection from others might lead to avoidance of seeking help (Komiya et al., 2000). The role of life circumstances of each individual and their personality traits cannot be ignored when making the decision to seek treatment. Any dependence on alcohol or drugs can effect seeking treatment as well.

Reaching an accurate diagnosis in psychiatry takes some time, due to some diagnostic criteria that require minimum duration of symptoms. In addition, overlapping symptoms between psychiatric disorders defies the accuracy of the diagnoses, particularly in the early phases of disorders (Isohanni et al. 1997, Moilanen et al. 2003). Psychiatric diagnoses usually are based on information collected from the patient and his family beside a clinical observation rather than

any biomarkers such as blood tests causing the diagnosis to be less objective and highly dependent on the ability and experience of the therapist.

A great number of researchers have investigated the link between worse results and duration of untreated psychosis (DUP) over the past 25 years or so (Crow et al. 1986; Rabiner et al. 1986; Johnstone et al. 1995). A meta-analysis that studied DUP in countries with low incomes stated that DUP tends to be longer in those countries (Chiliza et al. 2012).

Loebel et al (1992) presented a definition of duration of untreated psychosis that became accepted for the first time. Later on, many studies focused on studying DUP as predictors of the outcome in schizophrenia (Perkins et al. 2005). However most of the studies are based on clinical populations rather than general population.

3.4.2 Definition of duration of untreated psychosis

To date, there is lack of agreement regarding the definition of an onset of psychosis which is noticeable in many DUP studies (Keshavan & Schooler , 1992 ; Norman & Malla, 2001). Researchers are divided in their opinions of the DUP commencement, with scholars such as Verdoux et al. (1998, 2001) and Singh et al. (2005) assigning it to the initial observable symptom of psychosis, and scholars such as Addington et al. (2004) and Kay et al. (1987) believing that DUP should be linked to specified periods or durations. As Norman and Malla (2001) point out, there is no current consensus on how to define psychosis using specific illness characteristics. Most of the studies use positive symptoms (i.e. hallucinations and delusions),

however some studies includes thought disorder, disorganized and bizarre or catatonic behaviour (Ho et al, 2000; Keshavan et al, 2003).

Jackson and McGorry (2009) argue that there is no consensus among research papers regarding the cessation of DUP. Some, such as Norman and Malla (2001) suggest that DUP ceases once drugs are administered, and others, such as Craig et al. (2000) suggest that DUP ceases when the patient first becomes hospitalised for the illness.

3.4.3 Instruments for estimating DUP and their reliability

Not all DUP studies used a structured assessment to estimate DUP (Szymanski et al., 1996; Scully et al., 1997; Hass et al., 1998; Malla et al., 2002; Rosen and Garety, 2005).

Some studies used the Royal Park Multi-diagnostic Instrument (RPMIP). On the other hand, Ho et al (2000; 2003) used The Comprehensive Assessment of Symptoms and History (CASH) in both of his studies to define DUP.

3.4.4 Previous studies of duration of untreated psychosis

Duration of untreated psychosis is influenced by several factors such as social factors, clinical factors and pathway to care. The study to be presented in this thesis highlights the impact of both social factors and pathway to care on DUP in sample of Saudis schizophrenia patients. As such, the research into DUP discussed in this chapter will be split into two categories: I) social factor research; and II) the relationship between DUP and the clinical pathway.

3.4.4.1 Social and demographic factors

One recent British study compared patients who were suffering from their first psychotic experience, divided into two research groups according to their DUP (Thomas & Nandhra, 2009). The group with the longer DUP (>12 weeks) consist of (n=28) while the group with the shorter DUP (>12 weeks) consist of (n=46). Results showed that longer DUP was significantly associated with being a male and with less family support.

In terms of age, Dominguez et al. (2013) found that DUP in adolescence is greater than in adults (median DUP: adolescent = 179 days; median DUP: adults= 81 days). The findings support those of other researchers who attempted to evaluate the variances in results, baseline, and treatment between psychotic patients who developed the illness at an early stage (i.e. under 18 years of age) and those who developed the illness as adults aged older than 18 years. Those who had developed psychosis at a young age were shown to have a median DUP of 26.3 weeks and poorer performance prior to the onset of symptoms. On the other hand, those individuals who had developed the illness as adults performed better prior to the onset of symptoms and had a median DUP of just 8.7 weeks.

In a study from North America, a sample consisting of 242 patients with first-episode psychosis were examined in terms of demographic and clinical characteristics in two groups: adolescent-onset of psychosis (ages 15-18) and adult-onset of psychosis (ages 19-30). The early-onset group experienced longer DUP. (Ballageer et al., 2005)

The study by Fawzi et al (2011) is the only study from the Arab world regarding DUP and showed no significant association between any of the socio-demographic factors and DUP.

3.4.4.2 Pathway to care

There is increasing evidence that the pathway patients choose before seeking help from mental health services might be associated with DUP (Adeosun et al, 2013). Studies from Western countries showed that psychosis patients seek help first from psychiatric or other medical professionals (Anderson et al, 2010). This is probably has to do with the belief system in these communities. Patients and their relatives relate psychosis symptoms to medical or biological causes (Angermeyer and Matschinger, 1996; Minas et al., 2007). On the other hand, studies from Asia and Africa show that the first pathway for such patients is through non-physicians such as traditional healers, spiritual healers and religious people (Abiodun et al, 1995; Gureje et al, 1995; Chiang et al, 2005; Chong et al, 2005 Agara and Makanjuola, 2006).

The aim of Adeosun and co-workers (2013) in a study in Nigeria was to evaluate the most frequent first pathway to care among 138 schizophrenia patients. The results showed that the majority of the sample (69%) sought help first from traditional healers causing a longer DUP. Similar results emerged from the Agara and Makanjuola (2006) study. They found that around 70% of the patients sought help first from spiritual healers and 43% from traditional healers before seeking any medical help.

A comparative study was conducted in Zambia by Mbewe et al. (2006) between patients with long DUP and short DUP. The study results confirmed the impact of seeking help from traditional healers as the first pathway to care on DUP.

Two studies were conducted in the 90's .The first one was in the southwestern Nigeria (Gureje et al, 1995) while the second one was in north central Nigeria (Abiodun et al, 1995). Both studies suggested that the majority of psychosis patients contacted traditional and spiritual healers before seeking any medical help. In contrast to these previous studies, Chong et al .(2005) study in Singapore, noted that 24% of the study sample had pre-consultaion with traditional healer before seeking medical help however this had no effect on DUP.

From the Arab world Fawzi et al (2011) carried out a study that confirmed that the first pathway to care remains the most significant predictor for a long DUP. Their study was conducted on a total of 96 psychosis patients (50 Egyptians and 46 Saudis) and results showed that 78% from the Egyptian sample and 67% from the Saudi sample had sought help from traditional healers before going to a psychiatrist or any other medical professional. The prominent role played by traditional healers in primary psychiatric care was noted early on Okasha (1968). It could be possible that individuals in Saudi Arabia are hesitant to look for medical assistance for mental illnesses because there is little knowledge of it, and they may believe that supernatural powers like magic are the cause of these symptoms (Al-Subaie & Alhamad, 2000). This has been mentioned in more detail previously in Chapter 1 under the Saudi context.

On the other hand, Sharifi and co-workers (2009) conducted a study of first episode psychosis (FEP) inpatients in Iran and, unexpectedly, found that the median DUP was 11 weeks, thus comparable to that found in Western studies. Similar proportions of patients initially sought help from psychiatrists (n = 23, 25.3%) as from traditional healers (n = 21, 23.1%), with a smaller proportion seeking help first from a GP (n = 16, 17.6%) (Sharifi et al, 2009).

3.5 Conclusion

This chapter provides a comprehensive picture of the research literature on the epidemiology, symptomology and pathology of schizophrenia. While schizophrenia epidemiology, factor analysis and duration of untreated psychosis are all discussed in the literature, there is a serious shortage of studies from the Arab world in general and from Saudi Arabia specifically. The research reported in this thesis aims to take a step towards rectifying this situation. The following chapter will provide in detail the research design and methodology.

CHAPTER 4: METHODOLOGY

4.1 INTRODUCTION

This chapter will describe the original research that was carried out for the Ph.D. The choice of design, data collection in terms of hospitals included in the study, identification of potential patients with schizophrenia, diagnostic procedure, case ascertainment and ethical approval. As discussed above three separate analyses were carried out to address three areas of interest. Therefore, data management, data manipulation and statistical analysis will be described separately for each study (general epidemiology, factor analysis of OPCRIT items, and the DUP study).

4.2 STUDY DESIGN

The chosen study design was a retrospective case note study of all incident cases of schizophrenia over a 2 year period presenting in the capital city of Saudi Arabia. This choice can be explained by a number of reasons. Incidence studies are often conducted by identifying all new presentations of psychosis, usually with the cooperation of clinicians. This approach allows research interview data to be collected. It is however extremely resource intensive and simply was not possible for this Ph.D. An advantage of conducting a retrospective study is that basic information can be collected efficiently on a large number of people. Assuming adequate data storage very high levels of case ascertainment can be achieved without the necessity of approaching clinical teams.

Power calculations were carried out to determine the number of subjects needed to test the main hypotheses for the epidemiological study and two years data was sufficient.

Clinical and demographic data were collected from people who presented (as outpatients or inpatients) with psychotic symptoms across 6 hospitals in Riyadh between 2009 and 2011. During this period, all psychiatric services in Riyadh were provided by Ministry of Health (MOH) hospitals and other governmental hospitals.

Three analyses were carried out from the data collected:

4.2.1 Study I

The first study is an epidemiological study (ecological study), which determines the incidence of schizophrenia amongst the population in Riyadh and to identify associations between incidence of schizophrenia and demographic and socio-environmental characteristics.

4.2.2 Study II

The second study in this thesis is to evaluate the five factor model and its ability to distinguish unique and explanatory patterns among Saudi schizophrenia patients by factor analysis of OPCRIT items and testing if there is any association between the five factors and demographic data included in OPCRIT.

4.2.3 Study III

The third study is a descriptive DUP (duration of untreated psychosis) study which focused on describing the duration of untreated psychosis in the capital city of Saudi

Arabia and to identify any association between the DUP and both patients demographic factors and their first pathway to care.

4.3 STUDY POPULATION

The incidence, DUP and factor analytic studies were based on data from people aged 16-65 years who resided in the city of Riyadh, Saudi Arabia. Riyadh is divided into 5 areas, which comprise of 16 districts and 150 neighbourhoods as well as the Diplomatic Quarter. Patients were recruited over a 2-year period from the 1st January 2009 to the 1st January 2011. As I mentioned earlier in chapter 2 , the total population of Riyadh is 5.7 million inhabitants, Saudi citizens constituted 61% compared to 39% for non-Saudi. For Saudi population, the proportion of males is 52% (1,808,004) versus 48% for Saudi females (1,668,096). On the other hand, for non-Saudi population, the proportion of non-Saudi males is 69% (1,533,008) while for females it is 31% (689,013) (see Appendix 2 for details of areas, districts and neighbourhoods included in the study).

4.4 MINISTRY OF HEALTH HOSPITALS AND OTHER GOVERNMENTAL HOSPITALS INCLUDED IN THE STUDY

The city of Riyadh is served by number of Ministry of Health (MOH) hospitals, and other governmental hospitals, which provide psychiatric services (inpatients and outpatients): two of them were excluded from this study. **Security Forces Hospital Program (SFHP)** was excluded because it does not accept patients with schizophrenia due to a lack of necessary psychiatric care for such cases. **King Fahd Medical City (KFMC)** also does not accept psychiatric patients, as they do not have a locked inpatient ward. They do not accept psychotic patients since they have partnered with Al Amal hospital to provide psychiatric care.

4.4.1 Ministry of Health (MOH) hospitals

The Amal Complex for Mental Health

It is a MOH governmental complex that includes two hospitals with multiple facilities. The first hospital specialises in mental illness and provides free therapeutic services for Saudis and non-Saudis. The second hospital provides treatment and therapy for patients who are suffering from addiction. The mental illness hospital opened in 1983, with a clinical capacity of 230 beds. The hospital provides psychiatric services for both in and outpatients. It is located in the west area in Riyadh in the district of Erga (neighborhood: Alkozama).

King Saud Medical City (KSMC)

It is one of the key portals among the group of providing healthcare services in the Kingdom. The hospital opened in 1956 and the Ministry of Health assumed responsibility for the operation and maintenance of it. KSMC is a well-known hospital with one on the best reputations in the Kingdom. The hospital only provides psychiatric services for outpatients. It is located in the centre of Riyadh in the district of Al Shmesi (neighbourhood: Al Shmesi).

4.4.2 Other governmental hospitals

King Abdulaziz Medical City (KAMC)

This is a military hospital in Riyadh. It opened in 1983 and has continued to grow, while providing services for a fast growing population in all of its catchment areas. It provides a full range of care to all National Guard soldiers and their families, whether it is only primary health care or even tertiary specialised care. It has been recognised as a distinguished healthcare provider and is located in the east area of Riyadh in the district of Al Slay (neighbourhood: Kashm Ala'n). This hospital provides psychiatric services for both in- and outpatients.

Prince Sultan Military Medical City (PSMMC)

This hospital opened in December 1978. It is approximately 20kms from Riyadh city centre, in the district of Al Malaz (neighbourhood: Alwazarat), which is easily accessible to the general population. PSMMC one of the most advanced medical centres in the Middle East. It is also a military hospital and is the medical services department of the Ministry of Defence and Aviation (MODA); it, therefore, provides medical services to MOD personnel and their families. This hospital provides psychiatric services for in- and outpatients.

King Faisal Specialist Hospital & Research Centre (KFSH&RC)

This is a 935-bed tertiary care hospital. It is a governmental hospital, which is based in the centre of Riyadh (neighborhood: Altakasosi). The hospital opened in 1975 and provides the highest level of specialised healthcare in an integrated educational and research setting. Despite being a government hospital, it is difficult to access without Royal permission and so most of its patients are members of the royal family or are important citizens within the country. Psychiatric services are only provided for outpatients.

King Khalid University Hospital (KKUH)

This hospital opened in 1982. It is a governmental teaching hospital with an 800-bed capacity that includes a psychiatric unit of 23 beds and large outpatient services. The hospital provides all general and subspecialty medical services. It provides primary and secondary care for the general population. The hospital is located in North Riyadh, in the district of Al-Dereyah.

All governmental hospitals that provide psychiatric services to the population of Riyadh were included in the study. Care is free and available to all (Saudi and non Saudi). However, women (Saudi or migrant) cannot get to the hospital unless a male relative takes them or unless they can arrange a taxi or private drivers.

4.5 IDENTIFYING PATIENTS WITH SCHIZOPHRENIA

People with any possible illness were identified from residents (as defined by the 2005 Census) of Riyadh in Saudi Arabia, who were aged 16 to 65 years, and presented at one of the six mental health service clinics or wards for the first time with psychotic symptoms during the study period (1st January, 2009 to 1st January 2011). This ensured as complete case ascertainment as possible. Cases were identified by generating a list of all patients (in and out patients) from each psychiatric computer records in all governmental hospitals included in this study serving the city of Riyadh from 2009. ICD-10 codes of F20-F29, and from F30-F32 (World Health Organization, 1992) were used to identify cases.

4.6 DIAGNOSTIC PROCEDURE

Cases were identified by ICD-10 codes of F20-F29, and from F30-F32. The records of outpatients were of a similar standard to the records of in-patients. Patients' records were also checked to ensure that they had not previously contacted a psychiatric service or received any treatment at another psychiatric facility. They were then rated using the Operational Criteria (OPCRIT) checklist by myself to determine ICD-10 schizophrenia diagnoses using the associated computer program.

4.7 CASE ASCERTAINMENT

Every case of potential psychosis making first contact with mental health services in the study catchment area was identified. In order to minimize under or over ascertainment inclusion criteria were used, this included:

i) Age 16-65 years

ii) Resident in Riyadh city

iii) ICD-10 diagnosis of schizophrenia.

iv) Absence of an organic or severe learning disability.

v) No previous contact with psychiatric services for psychotic symptoms.

Cases were analysed using the Operational Criteria (OPCRIT) checklist by the main researcher (myself) to determine ICD-10 diagnoses using the associated computer program

Cases of all nationalities were included but the analysis of OPCRIT factors and DUP were restricted to people of Saudi nationality.

4.8 STUDY ASSESSMENTS

Data relating to Clinical, demographic factors, Duration of untreated psychosis (DUP) dates and pathway to care were all extracted from patients' medical records using a semi-structured instrument (See appendix 3)

The instrument consist of the following:

1) Hospital / patient information (e.g. hospital name/type; case number; dates...)
2) Demographic Factors (e.g. nationality; gender; age (when contact- first onset); place of residence; place of origin…)

3) Psychiatric History (e.g. reasons for consultation; early manifestation of the illness; time and mode of onset…)
4) Family History (e.g. family member (parents and siblings –spouse and children); premorbid personality…)
5) Pathway to care (e.g. where did the patient go first for help?)

4.8.1 The Operational Criteria Checklist for Psychotic Illness ratings (OPCRIT)

OPCRIT (Operational Checklist for Psychotic Symptoms) (McGuffin, Farmer and Harvey, 1991) has been used extensively as a tool for characterising forms of mental illness, therefore it has been used heavily in different types of research. The Operational Checklist for Psychotic Symptoms consists of a 90-item checklist based on operational criteria for the major psychiatric classification systems associated with a computer program (Appendix 3) It contain a lexicon of clear and descriptions of each major item and instructions for coding them. Diagnoses are based on 13 different operational diagnostic systems including the following:

1) DSM-III (American Psychiatric Association, 1980)
2) DSM-III-R (American Psychiatric Association 1987)
3) DSM-IV (American Psychiatric Association 1994)
4) ICD-10 (World Health Organization 1993)
5) Research Diagnostic Criteria (RDC) (Spitzer et al. 1978)
6) St. Louis criteria (Feighner et al. 1972)
7) The "flexible" criteria for schizophrenia (Carpenter et al, 1976)
8) Schneider's first rank symptoms (Schneider, 1959)
9) Taylor and Abrams criteria (Taylor and Abrams 1978)
10) A version of the French criteria for non affective psychosis upon the writings of

Pull et al (1987) in McGuffin & Murray (2013).

11) Sub-type classification of schizophrenia (Tsuang and winokur, 1974)

12) Sub-type classification of schizophrenia (Crow, 1980)

13) Sub-type classification of schizophrenia (Farmer et al, 1993)

Skilled clinicians are able to complete the OPCRIT checklist based on information extracted from different sources such as interviews and case records. Many studies had reported reliability of OPCRIT ((McGuffin et al. 1991, Craddock et al. 1996, Cardno et al. 1996, Azevedo et al. 1999)

For this study the OPCRIT checklist and associated computer program were used to determine ICD-10 schizophrenia diagnoses in order to maximize the diagnostic objectivity.

The OPCRIT items were also analyzed in order to describe symptom dimensions among schizophrenia patients.

4.9 ETHICAL APPROVAL

Ethical approval for this study (PNM/11/12-62) was granted from Kings College London in May 2012. Another ethical approval (IRB-079) was granted from the Institutional Review Board (IRB) in the Ministry of Health (MOH) Saudi Arabia in September 2012. The next step involved submitting an ethics application to every appropriate Research Ethics Committee in Riyadh's hospitals within this study. Approval to undertake this study and collect full demographic and diagnostic data from patient's medical files was granted from all of the hospitals (see Appendix 2 for more details relevant to the ethical approval).

4.10 DATA MANAGEMENT AND STATISTICAL ANALYSIS

4.10.1 ANALYSIS I – Descriptive epidemiology of schizophrenia in Riyadh

4.10.1.1 Data Management

I. Neighbourhood-level Variables

Information on neighbourhood characteristics was obtained from the 2005 Saudi Census. Information on population demographic characteristics of Riyadh was obtained from the Saudi Arabian Central Department of Statistics and information. The population data were broken down by nationality (Saudis and non Saudis), gender, and age broken down into 10 years bands and the income status across Riyadh neighbourhood. Unemployment rate and population density were not available across Riyadh neighbourhoods; however it was available across Riyadh districts instead. Marital status for women and men were available for Riyadh as a whole.

II. Individual-level Variables

Data on the cases were cleaned and checked and detailed tables constructed with the following variables: 1) place of residence (district), 2) place of residence (neighbourhood), 3) nationality, 4) gender, 5) age at first contact, 6) income, 7) employment status, and 8) marital status.

III. Data manipulation

The data was manually entered from patient records into a Microsoft Excel spread sheet that was then read into STATA using the INSHEET command. There were several data set , OPCRIT items, population based grouping and all of the statistical analysis was conducted using STATA version 12.0 (Stata Corp LP, Texas USA).

Variables were recorded as follows:

1. Nominal categorical variables such as 'hospital name' was numerically coded into six levels: (1= The Amal Complex for Mental Health , 2= King Saud Medical City (KSMC) , 3= Prince Sultan Military Medical City (PSMMC) ,4= King Abdulaziz Medical City (KAMC), 5= King Faisal Specialist Hospital & Research Centre (KFSH&RC), 6= King Khalid University Hospital (KKUH)).
2. 'Hospital type' was categorised into 1=Military and 2=Non-military hospitals.
3. Place of residence was categorized in two part. Neighbourhood level was arranged from 1 to 150 neighborhoods. Districts were organized from 1-16 districts.
4. Nationality categories were divided into Saudis (1) and non-Saudis (2)
5. Gender categories were divided into Male (1) and Female (2)
6. Age was converted into 5 10-years age bands (1 = 16-25, 2 = 26-35, 3 = 36-45, 4 = 46-55, 5 = 56-65).
7. Monthly income was classified into 3 categories (1=less than 8000SR/per month, 2= between 8000SR-16000SR/ per month, 3=more than 16000/per month)
8. Marital status was classified into 3 categories (1= Single, 2=Married, 3= Divorced). The numbers of separated and widowed patients were very small.
9. Employment status was classified into 2 categories (1= Not employed and 2=Employed).

   Hence a dataset was created with number of cases in each population grouping.

4.10.1.2 Statistical Analysis

I. Rates of Schizophrenia in each district

To address the first question, the crude incidence rates of schizophrenia were calculated for each of the 16 districts. To allow more accurate comparison between the rates, the crude incidence rates were then adjusted for variances in the age and gender structure of the population of each district by direct standardisation to the population structure of Riyadh city according to the 2005 census. The standardised rate is defined as a "the overall rates that would have prevailed in the population being studied if the age and gender structure had been the same as the standard population". This analysis was carried out using the 'dstdize' command in STATA. Theses standardized incidence rates (SIRs) and their 95% confidence intervals were calculated to allow comparison with other studies.

II. Individual and Area Level Predictors of Variation in Incidence of Schizophrenia

A Negative Binomial regression analysis was conducted to examine the distribution of schizophrenia within Riyadh districts by the variables of nationality, gender, age, income level, unemployment status, population density, and marital status. The negative binomial regression is a generalization of Poisson regression, which is used to model the parameters of over-dispersed count data, which is when the conditional variance exceeds the conditional mean. It is also used to model count variables. Different negative binomial regressions were generated to determine the impact of nationality, gender, age, income, unemployment, population density, and marital status to the incidence rates of schizophrenia. Level of significance values of 0.05 were used in each of the negative binomial regressions. Statistical significance exist

is deemed to exist if the *P*-values were less than or equal to the level of significance value.

The analysis was designed to address the following questions:

- Does the rate of schizophrenia differ between Riyadh districts?
- Does the incidence of schizophrenia increase with increasing population density?
- Is the incidence of schizophrenia predicted by the individual and area level variables: migration, male gender, single status, lower social class and unemployment?

4.10.1.3 Software

The data were manually entered from patient records into Microsoft Excel spread sheet. Then, the data were exported to STATA statistical software for the statistical analysis. STATA TRANFER was used to convert finalised datasets to STATA version12.0 (Stata Corp LP, Texas USA).

4.10.2 ANALYSIS II: Factor Analysis of Schizophrenia symptoms and signs and their relation to demography in a Saudi Sample

4.10.2.1 Data management

- **Symptom ratings**

Information was extracted from patient's medical files. Due to reasons of geography and the nature of this study The OPCRIT checklist was completed from the case notes by the main researcher (myself) only (after being trained by my first supervisor, Jane Boydell). OPCRIT is a 90-item checklist for psychotic and affective symptoms. It is widely used as a polydiagnostic assessment tool with a good reliability and validity (Azevdo et al., 1999; Craddock et al., 1996).

4.10.2.2 Statistical Analysis

I. Selection of symptoms for entry into factor analysis

Firstly, the 16 patients history items were excluded from the total 90 items leaving 74 OPCRIT items, following Allardyce "Irrelevant items to phenomenology were excluded, or where it would be hard to decide if they were primary or in fact, secondary to medication (initial/middle insomnia, excessive sleep, reduced concentration, slowed activity, loss of energy, increased appetite, weight gain/loss)" were excluded (Allardyce et al, 2007, p 430). Finally, The total left was 51 OPCRIT items, which were entered into factor analysis (more details are provided in chapter 6)

II. Exploratory factor analysis

Exploratory factor analysis (EFA) was chosen for this study to explore the underlying dimensions rather than testing previous developed model. Among the 51 OPCRIT items, some of them were 3 or 4 scale ordinal items and others were binary items. We initially ran analysis for three through six factors based on previous studies (Demjaha et al, 2009) and decided upon the five-factor solution as it had very good interpretability of the factors. In addition, we inspected the factor solution by the "eigenvalue greater than 1" rule, and the scree plot to guide the number of factors to include in the model. These were subjected to oblique (promax, correlated) rotation to find a solution with the best simple structure, that is, a pattern of results such that each variable loads highly onto one and only one factor. In other words, only items with robust loadings of greater than 0.4 were used (Dikeos et al, 2006; Demjaha et al, 2009). Regression factor scores were then calculated based on the factor loadings of that rotation.

III. The relationship of dimensions to known demographic/premorbid risk factors

After we determined the number of factors, we fitted a series of linear/logistic regression models, with the dimensional scores as the independent variables and each demographic/pre-morbid factor as the dependent variable: gender, age at onset, marital status, unemployment at onset, poor pre-morbid social adjustment, premorbid personality disorder, alcohol and drug abuse within one year of onset of symptoms, a definite psychosocial stressor prior to onset, family history of schizophrenia, family history of other psychosis. Poor work adjustment and coarse brain disease prior to onset.

The analysis was designed to address the following questions:

- What is the OPCRIT dimensional structure for Saudi schizophrenia patients?
- Is there a correlation between social and demographic data included in OPCRIT (sex / age / family history (psychosis / schizophrenia) / use of drugs /alcohol / social status / premorbid personality disorder/ psychosocial stressor prior to onset) with factors scores on the OPCRIT?

4.10.2.2 Software

Statistical analyses were performed using SAS version 9.2 (SAS Inc. Cary, NC, USA). All tests done when necessary were 2-tailed with an alpha level of 0.05.

4.10.3 ANALYSIS III: Duration of untreated psychosis and pathway to care in Riyadh, Saudi Arabia

4.10.3.1 Data Management

I. Duration of untreated psychosis

Information was extracted from 421 patients' psychiatric records in order to verify dates about the onset of symptoms and treatment. Among 421 patients, 211 records had date of onset given in up to day and 210 patients had date of onset given in up to month so an approximated date for them with 1 for a day was used. Maximum discrepancy from a true value can be 0.083 year (=30 days). For the end point all records specified this up to day.

II. Independent variables

All independent variables (except age at onset) are binary categorical variables:

1-'Marital status' was classified to (1=Married, and 2="Single and Other") which includes single, divorced, separated, and widow, and they were joined together due to the small numbers of separated and widowed.

2- 'Level of education' was classified in to two categories (1= School and lower, 2=University and higher)

3- 'Monthly income' was classified into two categories (1= 8000SR per month or higher, 2=Less than 8000SR per month).

4- 'Family size' was classified into two categories (1=1-8 members, 2=more than 8 members).

5- 'Living status' was classified into two categories (1= with family 2= "Alone or other"), which included alone, prison, social institution and other.

6- Pathway to care was classified into two categories (1= Psychiatric and non-Psychiatric Health Profession, 2= Traditional Healer and Other), which included traditional healer, and religious person.

4.10.3.2 Statistical analysis

Survival analysis was used to analyse the relationship between DUP and other variables. The onset of psychosis is chosen as the entry point and the contact with services is as the end-point. The associations between DUP and both demographic factors and pathway to care were carried out using Wilcoxon rank-sum test. Further investigations were made using Kaplan–Meier survival curves, log-rank tests and Wilcoxon tests to assess differences between groups in the survival probability. Only variables with significant association were included to be examined in the Cox proportional hazard regression.

The analysis was designed to address the following questions

- Is there a significant association between DUP and age, gender, marital status, education level, employment, socioeconomic status, substance misuse and pathway to care?

4.10.3.3 Software

All analyses were conducted using SAS version 9.2(SAS Inc. Cary, NC, USA). All tests were 2-tailed.

4.11 CONCLUSION

This chapter has provided detailed information about the research methodology. Due to the nature of this research, I initially presented the standard procedures that

I followed in collecting the date then I mentioned both data management and statistical analysis for each analysis separately. The next chapter will provide the results from study I of this research " Epidemology of schizophrenia in Riyadh, Saudi Arabia" in a paper format, arranged into introduction, methods, results and discussion.

CHAPTER 5: STUDY I- Epidemiology of Schizophrenia in Riyadh, Saudi Arabia

5.1 OVERVIEW

The distribution of schizophrenia has never been described in an Arabian country and the ecological associations, relatively recently identified in the West, have not been tested in Arabic culture. The aim of this study is to describe schizophrenia incidence in Riyadh (capital city of Saudi Arabia) and then test whether variation occurs according to nationality, sex, age, marital status, employment status, neighbourhood, area level income and population density. 435 new cases of schizophrenia between 2009 and 2011 were identified from all the hospitals in the study. Negative binomial regression analysis was conducted to investigates the incidence of schizophrenia in Riyadh and then to test whether variation occurs according to demographic variables and population density. Results showed that schizophrenia incidence rate varied greatly across the 16 Riyadh districts, the rate was higher within the younger population group, for Saudi than non-Saudi, for male than female and among unemployed than employed. In terms of marital status, rates were highest among divorced and separated people and higher amongst single compared to married people. The results of this study demonstrate similar effects of young age population, male gender, single status and unemployment being associated with higher rates of schizophrenia, as found in the West. It also reveals a lack of association between population density and schizophrenia incidence; this is in contrast to Western studies.

5.2 Introduction

Schizophrenia is a severe disease of the brain and mind, which affects approximately 1% of people worldwide (Minzenberg et al., 2008). Many epidemiological studies which were conducted in Western countries showed that the incidence of schizophrenia was associated with different neighbourhood characteristics such as social and economic status (Faris and Dunhum, 1939; Clark, 1949; Hare, 1956b) ethnic minority proportions (Halpern, 1993; Boydell et al., 2001), inequality (Boydell et al., 2004) and deprivation (Croudace et al., 2000). Many of these studies reported that schizophrenia rates tend to be higher in city rather than rural areas. Studies describing the incidence of schizophrenia in Saudi Arabia are rare, and the few studies that have been published tended to focus on issues associated with schizophrenia rather than the epidemiology (Zarroug, 1975; Chaleby & Tuma, 1987; Kent & Wahass, 1996). Therefore, this study aimed to describe the incidence of schizophrenia in Riyadh, Saudi Arabia in terms of age, gender, marital status, employment status and nationality/migration. A second aim was to use the incidence data to demonstrate heterogeneity across districts in Riyadh and test whether deprivation and population density explained some of the variation after adjusting for individual level factors.

5.3 Methods

5.3.1 Catchment area

Riyadh is the Capital of Saudi Arabia and has a population of nearly 5 million (CDSI, 2010). For administrative purpose it is divided into 16 districts, which were used as units to study variation in incidence of schizophrenia across Riyadh. The city of Riyadh is served by number of Ministry of Health (MOH) hospitals and other governmental hospitals, which provide psychiatric services. Hospitals included in this study were: The Amal Complex for Mental Health, King Abdulaziz Medical City (KAMC), Prince Sultan Military Medical City (PSMMC), King Saud Medical City (KSMC) , King Faisal Specialist Hospital & Research Centre (KFSH&RC), King Khalid University Hospital (KKUH).

These provided comprehensive coverage of all admissions, as there are no private inpatient services in the capital. Near complete ascertainment of all outpatient contacts was also achieved as these hospitals provide almost all-psychiatric care.

5.3.2 Population at-risk

I used the 2005 Saudi Census to estimate the population at-risk. Information on population and demographic characteristics of Riyadh was obtained. The population data were broken down by nationality (Saudis and non Saudis), gender, and age in 10 years bands (from 16-25). Income was used as a measure of wealth/deprivation of Riyadh neighbourhoods. Unemployment rates and population density were available districts level. Marital status for women and men was available for Riyadh as a whole.

5.3.3 Identification of participants

People with any possible psychotic illness were identified from residents (as defined by the 2005 Census) of Riyadh in Saudi Arabia, who were aged 16 to 65 years, and presented, at one of six mental health service clinics for the first time with psychotic symptoms during the study period (1st January, 2009 to 1st January, 2011). I identified cases by generating a list of all patients (in and out patients) from each psychiatric hospital computer records in all governmental hospital included in this study serving the city of Riyadh from 2009. ICD-10 codes of F20-F29, and from F30-F32 (World Health Organization, 1992) were used to identify potential cases.

5.3.4 Diagnostic procedure

After identifying cases with ICD-10 codes, the records of patients with psychotic symptoms were further examined to identify those who made contact with health services but were not admitted. The records of patients who were not admitted were of a similar standard to the records of those admitted. Patients' records were also checked to ensure that they had not previously contacted a psychiatric service or received any treatment at another psychiatric facility. They were then rated using the Operational Criteria Checklist (OPCRIT) to determine ICD-10 schizophrenia diagnoses using the associated computer program.

5.3.5 Selection of individual and area level predictors of incidence

The selection of potentially relevant individual and area level factors was based on the literature review; this was limited by the availability of data from the Saudi Arabia Central Department of Statistics & Information. The following are the independent variables included in the study:

- Age has been considered as a risk factor for schizophrenia incidence in a large number of studies (with higher risk in younger adults), therefore age in 10 year groupings from 16-25, was included in this study (Ochoa et al, 2012).
- Gender differences in the incidence of schizophrenia have been subject to debate in the literature. Several studies reported that men had higher incidence than women (Lewine et al. 1984; Aleman et al. 2003) particularly when a narrower definition is used.
- Migration has been consistently found to be a risk factor for psychosis and increased incidence has been found in many minority groups (Boydell, 2001; Selten, 2001; Fearon, 2006) Saudi and non Saudi nationality was used to capture this effect as population data was available at this level. People with non-Saudi nationality were also migrants, mostly migrant workers.
- Marital status was included because its association with schizophrenia is consistently found in the literature in that single people have higher rates (Malzberg, 1936; Dunham, 1966; Turner et al, 1970).). Population data was available broken down into married, divorced, widowed and single (never married) by age (10 year bands) and gender for the whole of Riyadh.
- Population density, which was defined in this study by persons per square kilometre within districts of Riyadh. An association between population density and higher rates of schizophrenia has been repeatedly found in the literature (Van Os et al. 2003; Sundquist et al.2004, Weich et al. 2006; Dekker et al. 2008)

- Monthly income per household was included in this study as an indicator of wealth of an area as studies have indicated a negative association between economic prosperity and the occurrence of mental illness (Weich et al, 2006; Sundquist & Ahlen, 2006) and schizophrenia (Sariaslan et al, 2014).
- Unemployment was included because it has been found to be an individual and area level predictor of increased schizophrenia incidence (Henderson et al, 1998; Zimmerman & Katon, 2005; Fortney et al, 2007,2009; Jia et al, 2009; Marwaha et al .2009; Boydell et al 2013)

5.3.6 Statistical analysis

I. 5.3.6.1 Variable coding

Data

The case and population data was stratified by nationality (Saudis and non Saudis), gender, and age in 10 years bands. Data was entered by neighbourhoods, within districts. Median income status was entered by neighbourhood. Unemployment rate and population density were not available at neighbourhood level and so were entered by district. Marital status for women and men were available for Riyadh in general so this was analyzed separately.

5.3.6.2 Statistical methods

Direct standardization (using the entire population as the standard) was used to calculate standardized incidence rates for the districts and neighborhoods. Standardization was by age and gender.

A Negative Binomial regression was conducted to test the distribution of the schizophrenia illness within Riyadh districts by the variables of nationality, gender, age, income level, unemployment status, population density, and marital status. The negative binomial regression is a generalization of Poisson regression, which is used to model the parameters of over-dispersed count data, which is when the conditional variance exceeds the conditional mean. It is also used to model count variables. Different negative binomial regressions were generated to determine the impact of nationality, gender, age, income, unemployment, population density, and marital status to the incidence rates of schizophrenia. Level of significance values of 0.05 were used in each of the negative binomial regressions. Statistical significance exist if the *P*-values were less than or equal to the level of significance value.

The data was manually entered from patient records into Microsoft Excel spread sheet. Then, the data were exported to STATA statistical software for the statistical analysis. STAT TRANSFER was used to convert finalised datasets to STATA version12.0 (StataCorp LP, Texas USA). These datasets were used for all descriptive and the negative binomial regression analytical analyse

5.4 Results

5.4.1 Sample

The final sample consisted of 435 schizophrenia patients for the period 2009- 2011. Out of the 435 patients with schizophrenia 70% (n=306) were men, which is more than twice the number of women (n=129, 30%). Mean age at first contact was 28 years (IQR: 23-33 years) .The majority of patients 97% (n=421) were of Saudi nationality. More than half of the patients 56% (n=244) were single and around a third 32% (n=137) were married, 12% (n=51) were divorced. 75%of patients

(n=328) were educated to school level only, while 20% (n=84) had a university education. However 66% (n=285) were unemployed and 62% (n=268) had a monthly income less than 8,000 SR per month (note that the Central Department Of Statistics & Information indicated that the median monthly income in Riyadh is 13,000 SAR). Family size tended to be larger (more than 8 members) (n=186, 43%) and 90% (n=391) of patients lived with their family (according to ADA, the average number of family members is 6.3). One fifth (n=89, 21%) had a history of drug abuse. The total population at risk was about 3.420.000 (i.e. 16-65 over 2 years. The overall incidence was 12.7 per 100.000. Incidence in Saudi people was 20.2 per 100.000 and in non-Saudi people 0.9 per 100.000.

Table 5.1 Characteristics of the 435 schizophrenia patients

	n	Mean/[%]	(IQR)
Age (years)	435	28	(23, 33)
Age categories			
16-25 years	152	[34.9]	
26-35 years	194	[44.6]	
36-45 years	62	[14.3]	
46-59 years	27	[6.2]	
Gender			
Female	129	[29.7]	
Male	306	[70.3]	
First episode (year)			
1999	1	[0.2]	
2000	8	[1.8]	
2001	5	[1.2]	
2002	9	[2.1]	
2003	16	[3.7]	
2004	18	[4.1]	
2005	27	[6.2]	
2006	40	[9.2]	
2007	70	[16.1]	
2008	59	[13.6]	
2009	88	[20.2]	
2010	68	[15.6]	
Missing	26	[6.0]	
First diagnosed (year)			
2009	218	[50.1]	
2010	217	[49.9]	
Nationality			
Saudi	421	[96.8]	
Non-Saudi	14	[3.2]	
Marital status			
Single	244	[56.1]	
Married	137	[31.5]	
Separated	2	[0.5]	
Divorced	51	[11.7]	
Widowed	1	[0.2]	
Education level			
Illiterate	16	[3.7]	
School education	328	[75.4]	
University education	84	[19.3]	
Missing	7	[1.6]	
Employment status			
Not employed	285	[65.5]	
Employed	150	[34.5]	

Monthly income		
Less than 8,000 SR per month	268	[61.6]
8,000 to 16,000 SR per month	103	[23.7]
More than 16,000 SR per month	61	[14.0]
Missing	3	[0.7]
Family size		
1-4 members	93	[21.4]
5-8 members	152	[34.9]
More than 8 members	186	[42.8]
Missing	4	[0.9]
Living status		
Alone	21	[4.8]
Family	391	[89.9]
Family in-law	3	[0.7]
Other	17	[3.9]
Missing	3	[0.7]
Drug abuse		
No	346	[79.5]
Yes	89	[20.5]

- **Crude and Adjusted Incidence Rate of Schizophrenia across Riyadh Districts**

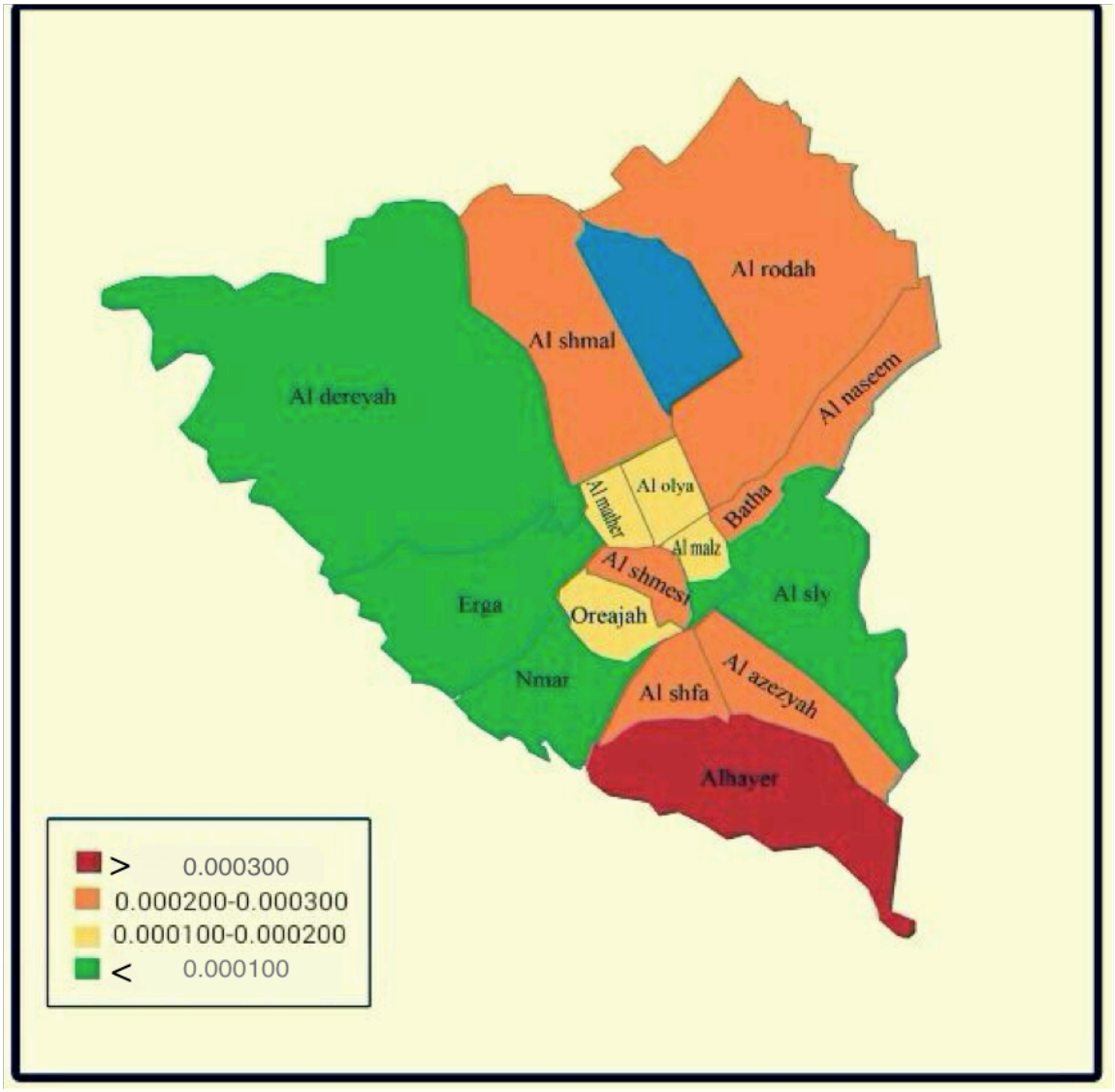
To address the question of variation in incidence across districts, the crude incidence rate of schizophrenia was calculated for each district. The crude incidence rates for schizophrenia in each district are summarized in Table 5.2.

The crude incidence rate varied greatly across the 16 Riyadh districts. The results showed that the highest crude incidence rate was the Riyadh district of Al-Hayer (11) with the crude rate of 37.5 and the lowest crude incidence rate was the Riyadh district of Nmar (7) with the crude rate of 0 .The incidence, standardised for age and gender, also varied from 0.00 to 37.1 per 100 000 person years suggesting considerable variation in incidence that is not attributable to population structure.

Table 5.2 Crude and Standardised Rates of Schizophrenia by Riyadh District

District	N	Cases	Crude	Adj Rate (95% CI)
Al-Shmal	6149	18	29.2	29.6 (15.9 -43.3)
Al-Dereyah	33285	2	6	6 (0 -14.2)
Al-Rodah	295918	61	21	20.9 (15.7 -26.2)
Al-Naseem	333631	85	26.1	26.6 (21- 32.2)
Alslay	217521	17	7.8	7.6 (3.9 - 11.3)
Erga	96600	5	5.2	6 (0.6 - 11.3)
Nmar	33788	0	0	0 (0)
Al-Oreja	315334	47	14.9	14.7 (10.4 - 19)
Al-Azezy	71627	16	23.7	23 (12.1 - 33.9)
Al-Shfa	119976	29	24.2	24.3 (15.4 - 33.1)
Al-Hayer	13319	5	37.5	37.1 (4.6 - 69.5)
Al-Olyah	290120	30	10.7	10.9 (7 - 14.7)
Al-Mather	87812	18	17.1	16.7 (82 -25.2)
Al-Malz	239050	39	15.9	15.7 (10.6 - 20.9)
Al-Shmesi	185039	41	22.2	23.9 (16.5 - 31.3)
Al-Batha	330578	22	4.8	5.4 (2.7 - 8.1)

Figure 5.4 Riyadh Map: Crude Incidence Rate of Schizophrenia by Riyadh District



3 5.4.3 Individual and Area Level Predictors of Variation in Incidence of Schizophrenia

I. Variation in Incidence Rates of Schizophrenia by Age, Gender, Nationality, Unemployment, and Population Density

Poisson regression was considered for the analysis. The incidence data however was over dispersed and therefore negative binomial regression was carried out. The results of the negative binomial regression to determine the effect of age, gender, nationality, unemployment, and population density on the incidence rates of schizophrenia in Riyadh are summarized in Table 5.3 .The results of the chi-square test, the test that all of the estimated coefficients are equal to zero, showed that the model is statistically significant (X^2 (5) = 246.14, P < 0.00).

On inspection

Of the negative binomial regression coefficients, all of the p-values for age (z= -5.41, P < 0.0001), gender (z= 4.81, P < 0.0001), nationality (z= 10.43, P < 0.0001), unemployment (z= 3.57, P < 0.0001), and population density (z= -1.99, P < 0.05) were all significant. These results indicated that the incidence rates of schizophrenia significantly differed by the age, gender, nationality, unemployment, and population density. Upon investigating the IRR coefficient, all the values were positive. The specific results were as follows:

- For age, the IRR of 0.67 indicates that for each one-unit (10 year age band) increase of the age, incidence of schizophrenia decreases by 0.67. This results means that the incidence of schizophrenia is lower for older aged population groups.

- For gender, the IRR of 2.34 indicates that for men had a 2.34 times higher incidence of schizophrenia than women.

- For nationality, the IRR of 26.41 indicates that people with Saudi nationality had 26.41 times higher incidence of schizophrenia than non-Saudis. This result means that the incidence of schizophrenia is higher for Saudis than non-Saudis; but please see limitations

- For unemployment rate, the IRR of 1.03 indicates that each 1% increase in unemployment ratio is associated with an increase in the incidence of schizophrenia by a factor of 1.03. This result means that the incidence of schizophrenia is higher for those that are unemployed than those that are employed.

- For population density, the IRR of 0.97 indicates that for each increase in the number of inhabitants per square kilometer, the incidence of schizophrenia decreases by 0.97. This result means that the incidence of schizophrenia is lower for areas that are heavily populated; but this was not statistically significant.

Table 5. 3 Incidence Rates Ratios of schizophrenia by Age, Gender, Nationality, Unemployment and Population Density

Variable	IRR[1]	Std.Err[2]	Z[3]	p[4]	95% CI[5]
Age[6]	0.67	0.05	-5.41	<0.001	0.58-0.77
Gender[7]	2.34	0.42	4.81	<0.001	1.66 -3.32
Nationality[8]	26.41	8.28	10.43	<0.001	14.28- 48.84
Unemployment Rate[9]	1.03	0.01	3.56	<0.001	1.02-1.05
Population Density[10]	0.97	0.01	-1.99	<0.05	0.94-1.00

Likelihood-ratio test of alpha= 0.00; X^2 (01) = 298.40 ,$p < 0.00$
Dispersion = mean
Log likelihood= 801.29
Number of obs= 3020
LR X^2(5) = 246.14
$p>X^2$ = 0.00
Pseudo R^2 = 0.13

[1] Incidence rate ratio
[2] Standard Errors
[3] Test statistic
[4] P-value
[5] Confidence Interval
[6] The younger age group 16-25 years was used as the reference group.
[7] Male was used as the reference group.
[8] Saudi was used as the reference group
[9] The estimated rate ratio comparing unemployed to employed, given the other variables are held constant in the model.
[10] The estimated rate ratio comparing heavily populated areas to less populated areas , given the other variables are held constant in the model

II. *Negative Binomial Regression Results of Effect of Age, Gender, Unemployment, and Population Density on Incidence Rates on Schizophrenia restricted to the Saudi Population*.

The results of the negative binomial regression to determine the effect of age, gender, unemployment, and population density on the incidence rates of schizophrenia for Saudis in Riyadh were summarized in Table 5.4 .The results of the chi-square test, the test that all of the estimated coefficients are equal to zero, showed that the model is statistically significant (X^2 (4) = 61.634, $P < 0.00$).

Upon the analysis of the negative binomial regression coefficients, all of the p-values for age (z= -5.26, $P < 0.00$), gender (z= 4.67, $P < 0.00$), unemployment (z= 2.86, $P < 0.00$) were all significant, except for population density (z= -1.41, $P < 0.16$). These results indicated that the incidence rates of schizophrenia significantly differed by the age, gender, and unemployment. Population density was not significantly associated with higher incidence of schizophrenia. Upon investigating the IRR coefficient, all the values were positive. The specific results were as follows:

- For age, the IRR of 0.67 indicated that for each one-unit (10 year age band) increase of the age, incidence of schizophrenia decreases by 0.67. This results means that the incidence of schizophrenia is lower for the older population Saudi group.

- For gender, the IRR of 2.32 indicated that for each one-unit (male gender) increase of the gender**,** the incidence of schizophrenia increases by 2.32. This result means that the incidence of

schizophrenia is higher for Saudi males, than Saudi females.

- For unemployment rate, the IRR of 1.03 indicated that that for each 1% increase on the unemployment ratio is related to an increase in the incidence of schizophrenia by 1.03. This result means that the incidence of schizophrenia is higher for those that are unemployed than those that are employed.

Table 5.4 Incidence Rates of Schizophrenia for Saudis by Age, Gender, Unemployment and Population Density

Variables	IRR	Std.Err	Z	p	95% CI
Age	0.67	0.05	-5.26	<0.001	0.58 - 0.78
Gender	2.32	0.42	4.67	<0.001	1.66 - 3.30
Unemployment Rate	1.03	0.01	2.86	<0.001	1.01 - 1.05
Population Density	0.98	0.02	-1041	0.16	0.95 - 1.00

Likelihood-ratio test of alpha= 0.00; X^2 (01) = 292.57,$p < 0.00$
Dispersion = mean
Log likelihood= -735.65
Number of obs= 1510
LR $X^2(5)$ = 61.63
$p > X^2$ = 0.00
Pseudo R^2 = 0.04

I. Incidence Rate Ratios of Schizophrenia in Single, Divorced and Married Saudi Women

The results of the negative binomial regression to determine the effect of marital status on incidence rates of schizophrenia in Saudi are summarized in Table 5.5.

The results of the chi-square test showed that the model is statistically significant (X^2 (3) = 11.08, P = 0.01) since the p-value was less than the level of significance of 0.05 indicating that the incidence rates of schizophrenia were significantly different between by marital status. The IRRs are reported for single and divorced women with married women as the reference. Upon the analysis of the negative binomial regression coefficients, all of the P-values for single women (z= 2.17, P < 0.03) and divorced women (z= 4.35, P < 0.00) were statistically significant. These results indicated that the incidence rates of schizophrenia significantly differed between married women and both single and divorced women.

Upon investigating the IRR coefficient, all the values were positive. However, the IRR coefficient of divorced women (8.07) was higher than that for single women (3.19). Thus, the result showed that the incidence of schizophrenia is higher among divorced and separated women than married. The IRR is 8.07 for divorced women compared to married women and 3.19 for single women compared to married women. The confidence intervals overlapped however. All results were adjusted for age.

Table 5.5 Negative Binomial Regressions Results of Difference of Incidence Rates of Schizophrenia between Divorced Women and Marred Women

Variables	IRR	Std.Err.	z	P	95% CI
Age	1.05	0.25	0.20	0.84	0.66- 1.68
Single status	3.19	1.71	2.17	0.03	1.12-9.13
Divorced or separated	8.07	3.88	4.35	0.00	3.15- 20.69

Married was used as the reference group
Likelihood-ratio test of alpha= 0.00; X^2 (01) =43.01 ,$p < 0.00$
Dispersion = mean
Log likelihood= -36.76
Number of obs= 12
LR $X^2(5)$ = 11.08
$p>X^2$ = 0.01
Pseudo R^2 = 0.13

II. Negative Binomial Regressions Results of the effect of marital status on incidence Rates of Schizophrenia on Saudi men

The results of the negative binomial regression to determine the incidence rate ratios of schizophrenia amongst divorced and single men compared to married men are summarized in Table 5.6.

The results of the chi-square test showed that the model is statistically significant (X^2 (3) = 17.51, $P < 0.00$) since the p-value was less than the level of significance of 0.05 indicating that the incidence rates of schizophrenia was significantly different between married and divorced men. Upon the analysis of the negative binomial regression coefficients, all of the *P*-values for single men (z= 5.36, $P < 0.00$) and divorced men (z= 6.18, $P < 0.00$) were all significant. These results indicated that the incidence rates of schizophrenia significantly differed between single men compared to married men and divorced men compared to married men.

Upon investigating the IRR coefficient, all the values were also positive. However, the IRR was higher for divorced men (25.4) compared to married men than for single men compared to married men (12.16) although the confidence intervals overlap. Thus, the result showed that the incidence of schizophrenia was considerably higher were among divorced and separated men than married men. All results are adjusted for age.

Table 5.6 Negative Binomial Regressions Results of Difference of Incidence Rates of Schizophrenia between Divorced and Married Men

Variables	IRR	Std.Err.	Z	P	95% CI
Age	0.99	0.22	-0.07	0.95	0.64 – 1.53
Single marital status	12.16	5.67	5.36	<0.00	4.88 – 30.31
Divorced or separated	25.49	13.36	6.18	<0.00	9.12 – 71.22

Married was used as the reference group
Likelihood-ratio test of alpha= 0.00; X^2 (01) =144.82 ,p < 0.00
Dispersion = mean
Log likelihood= -42.28
Number of obs= 11
LR X^2(5) = 17.51
p>X^2 = 0.00
Pseudo R^2 = 0.17

III. Incidence Rate Ratios of Schizophrenia by Marital Status between Women and Men

The results of the negative binomial regression to determine the incidence rate ratios of schizophrenia by marital status between men and women are summarized in Table 5.7.

The results of the chi-square test showed that the model is statistically significant (X^2 (4) = 28.58, $P < 0.00$) since the p-value was less than the level of significance of 0.05 indicating that the incidence rates of schizophrenia was significantly different by marital status between men and women.

Upon the analysis of the negative binomial regression coefficients, the *P*-value for of gender (z= -2.08, $P < 0.04$) was significant. This indicated that the incidence rates of schizophrenia significantly differed between men and women.

The IRR was 0.51which indicated for women**,** schizophrenia decreases by a factor of 0.52. This is adjusted for age and marital status.

Table 5.7 Negative Binomial Regressions Results of Difference of Incidence Rates of Schizophrenia by martial status between Women and Men

Variables	IRR	Std.Err.	Z	P	95%CI
Age	1.05	0.19	0.27	0.79	-0.74 - 1.48
Female Gender	0.51	0.17	-2.08	<0.04	0. 27- 0.96
Single marital status	6.54	2.54	4.84	<0.00	3.06 – 13.98
Divorced or separated	13.23	5.09	6.71	<0.00	6.22 – 28.13

Likelihood-ratio test of alpha= 0.00; X^2 (01) =216.03 ,$p < 0.00$
Dispersion = mean
Log likelihood= -81.04
Number of obs= 23
LR X^2(5) = 28.58
$p>X^2$ = 0.00
Pseudo R^2 = 0.15

5.4.5 Incidence of Schizophrenia and Income

Variation in Incidence Rate Ratios of Schizophrenia by Monthly Income Level after adjusting for age, gender, unemployment and population density

The results of the negative binomial regression to determine the effects of monthly income level were summarized in Table5. 8.

(X^2 (5) = 62.24, P < 0.00) The results of the chi-square test, the test that all of the estimated coefficients are equal to zero, showed that the model is statistically significant since the p-value was less than the chosen level of significance of 0.05 indicating that the overall effect of monthly income level on the incidence rates of schizophrenia was significant.

Upon the analysis of the negative binomial regression coefficients, the *P*-value for income (z= -0.75, P = 0.45) was insignificant since it was greater than the level of significance value of 0.05. This indicated that the incidence rates of schizophrenia did not significantly differ by the monthly income level. Monthly income was classified into 3 categories (1=less than 8000SR/per month, 2= between 8000SR-16000SR/ per month, 3=more than 16000/per month). Thus, the incidence of schizophrenia was not higher in lower socio-economic groups.

Table 5.8 Negative Binomial Regressions Results of Difference of Incidence Rates of Schizophrenia by Monthly Income Level

Variables	IRR	Std.Err.	Z	P	95%CI
Age	0.67	0.05	-5.26	<0.00	0.58 - 0.78
Gender	2.31	0.42	4.66	<0.00	1.62 - 3.29
Income	1.00	0.00	-0.75	0.45	1.00 - 1.00
Unemployment rate	1.03	0.01	2.48	<0.01	1.01 - 1.05
Population density	0.98	0.01	-1.50	0.13	0.94 - 1.01

Likelihood-ratio test of alpha= 0.00; X^2 (01) =291.80 ,p < 0.00
Dispersion = mean
Log likelihood= -735.35
Number of obs= 1510
LR $X^2(5)$ = 62.24
$p>X^2$ = 0.00
Pseudo R^2 = 0.04

5.5 Discussion

5.5.1 Key findings

This is the first epidemiology study of schizophrenia incidence to investigate the effect of age, gender, nationality, employment status, income, marital status and population density across different districts in Riyadh, Saudi Arabia. The results of the analysis showed the following:

- Incidence rate of schizophrenia varied significantly across different Riyadh districts.
- For the whole data set (i.e. Saudi and Non Saudi) Incidence of schizophrenia was higher within the younger population group. It was also higher for Saudi than non-Saudi, for male than female and among unemployed than employed.
- For the Saudi population incidence of schizophrenia was higher within the younger population group. It was also higher for male than female and among unemployed than employed. There was no effect of population density.
- Incidence of schizophrenia was highest among divorced and separated people and higher amongst single compared to married people.
- Incidence of schizophrenia did not significantly differ by the monthly income level of the area.

5.5.2 Methodological consideration

5.5.2.1 Methodological weakness

As the study is retrospective, the available information was extracted from case records; this method is in line with Boydell et al (2001) study.

- This study relied on clinical diagnosis as the primary screen for inclusion in the operationalized diagnostic process. Diagnoses that might include any psychotic symptoms would have been included, for example bipolar disorder. Diagnoses without psychotic symptoms would not however have been included such as anxiety. This means that if patients concealed or clinicians did not elicit psychotic symptoms the case would have been missed from the incidence. It is not possible to quantify the extent of this but it should be noted that this could also occur in interview studies as well.

  The unreliability of psychiatric diagnosis has been and still is a major problem in psychiatry. There are two categories of causes for unreliability of psychiatric diagnosis. The first one are the factors related to the patient such as the patient's psychological state which may hinder the provision useful and reliable information to the clinician. In addition, the use of proxy information which can be incomplete or distorted. Therefore, clinical reports by concerned family can vary widely depending upon whether they have a primary or secondary role in the patient care. This can be influenced by cultural concerns as to the meaning of the psychotic symptoms, possibly dismissed as normal or hidden as considered shameful. This might have differed by factors investigated such as gender. On the other hand, there are factors related to the clinician, such as the clinician interview, clinician training and experience, also the reliance on observation

which is a core component in any mental state examination. Nevertheless, there remains the potential that the standard methods employed by clinicians to solicit information may in fact bias patient data.

- The use of case note records is also another weakness of this study as the individual symptoms may be variable recorded by different psychiatrists due to differences in clinician's methods, experiences and the standards of the Institution. Therefore, it should be taken into account that the accuracy of the case notes relied to a large extent on the accuracy of the psychiatrists. This is unlikely to be differential by exposures such as population density though.
  - The possible omission of cases in the private sector is also another possible weakness of this study.

5.5.2.2 Methodological strengths

- One of the strengths of this study is that it included not only admitted patients, but also all patients with less acute level symptoms who contacted any mental health services, which reduced selection bias.
- Private hospitals were contacted for the purpose of this study. Unfortunately, they did not allow access to patient files to collect the data. However, they indicated that most schizophrenia cases are not new, that they have been seen before in other hospitals or clinics. There are no private psychiatric in-patient facilities in Riyadh, ensuring that all psychiatric admission are represented in the study. In spite of that, there is the possibility that we lost some cases
- In the case of ambiguity in any of the patients records, I asked for a meeting with the patient's psychiatrist to discuss the patient case and clarify some ambiguities

and unclear points and this was done to achieve a clear description of the symptoms in order to complete the OPCRIT checklist.

- In addition, I ensured the objectivity of schizophrenia diagnoses by using Operational Criteria (OPCRIT) checklist and associated computer diagnoses.

II. 5.5.3 Comparison with other studies

I could not compare our results with any previous Arabic studies, as for the best of my knowledge there are no such studies previously conducted in any Arab countries.

5.5.3.1 Previous Western findings

The effect of individual-level male gender and younger age, were in the expected direction (Van Os et al, 2000; Boydell et al, 2001) in addition to the effect of unemployment (Boydell et al, 2013) and being divorced (Van Os et al, 2000). This study showed higher incidence rate for men (70%) similar to 61% and 57% for men in both Van Os and Boydell studies respectively. The mean age for this study was younger (28 years) while it was (35.5) in Van Os study and (34.5) in Boydell study.

This study confirms the effect of spatial and geographical variations in the distribution of schizophrenia. It shows that the incidence of schizophrenia varies between neighborhoods which is consistent with previous studies (Faris & Dunham 1939; Hare, 1956a/b; Van Os et al., 2000; Boydell et al., 2001) .The incidence rate in the current study varied widely from 0 to 37.1 per 100 000

persons-years comparing to Boydell's results (2001) (varied from12 to 38 per 100 000 persons-year), but less than Van Os's study (2000) (varied from 0 to 51 per 100 000 persons-year).

On the other hand, comparing to the AESOP findings, the incidence rate recorded in this study is lower than the incidence rate in South-East London (55 per 100,000 person years) but higher than both Nottingham and Bristol (25 per 100,000 person years and 22 per 100,000 person years, respectively)(Morgan et al, 2006).

The results for the distribution of schizophrenia cases confirm those of previous studies (Faris and Dunham, 1939; Hare, 1956). There are, however some differences. As in Faris and Dunham's study, the central area of the city showed a high rate of schizophrenia, but in Riyadh high rates occurred not only in the poor central area but also in the high socioeconomic central area , which is similar to what Hare (1956) found. However, it was difficult for this study to point to a common social factor in both areas such as high population density as Faris and dunham's study or high proportion of person living alone as in Hare study (1956) and Van Os et al study (2000) or the presence of minority ethnic groups as in Boydell et al (2001) study. The results did not show any effect for population density on the incidence rate, opposite findings regarding minority ethnic effect on the incidence rate (although this might not be reliable) and it was impossible to study the effect of proportion of person living alone due to the lack of relevant data and very few people live alone.

The distribution of rates across a city are thought to depend on disorganisation and other putative factors such as crime and these will vary by city. The peripheral areas of the city had low schizophrenia rates in Faris and Dunham's study (1939) , but not in our study or Hare's study(1956) . Our findings showed that remote southern areas of the city showed high rates of schizophrenia as opposed to the remote northwestern areas of the city and we do not have an explanation for this.

In order to explain this distribution of schizophrenia in poor and wealthy central areas of Riyadh, a number of possibilities should be considered. Firstly, the free treatment under the MOH and the other governmental hospitals in Riyadh might have helped to reduce the differences between rich and poor people in their methods of seeking medical help. Secondly, the internal migrations and residential mobility of patients might be important factors for this distribution (which has not been considered in the current study). A Saudi Study indicated that most of the first-generation internal immigrants constitute 91.5% of the families in the center areas of Riyadh. Most of these internal immigrants are coming from the South-West of Saudi Arabia (74.8 of households in center areas are coming from Jazan). The mean age of the internal immigrant when he came to the city of Riyadh was young (28.6 years). Economic factors are the most important reasons for migration to Riyadh, whether looking for work (82.5%), or moving away from inadequate public services (49%). This same study revealed that the main attractions for housing in central of Riyadh for internal migrants are economic factors in the first place (low rent 53% - low house prices 13.3% - monthly installments for rent 11.6%) and social factors in term of the presence

of relatives (35%) (Al-Nuaim, 2004). In developing countries, internal migration might have led to a rise in mental disorders. Furthermore the accompanying economic and social changes might have led to the high rates of mental illness. (Okasha, 2005).

5.5.3.2 Overall incidence rates

In this study, the overall incidence rate of schizophrenia after adjustment for age and sex, was 20.2 per 100 000 person-years. This is comparable with the very highest rates of schizophrenia previously observed in the United Kingdom in the AESOP study 20.1 per 100 000 in south London (2006). A systematic review of incidence rates in UK over a period of 60 years was conducted and results showed that the over all incidence of schizophrenia varied between studies in UK, ranging from 4.4/100.000 (Reay et al, 2010) to 33/100.000 (Gater et al, 1995)(Kirkbride et al, 2012). According to McGrath et al study (2008), the overall crud incidence estimate was 15.2 per 100.000, which is lower than our results. Furthermore, the Jablensky study (1992) reported lower rates of schizophrenia incidence compared to our study as well. In their study, the broader diagnostic criteria of schizophrenia ranged from 1.5 to 4.2 per 10 000 people, and the highest incidence rate was found in India, while the narrower diagnostic criteria of schizophrenia were all between 0.7 and 1.4 per 10 000 people. Other studies reported annual schizophrenia incidence per 1000 people as following, Aarhus, Denmark 0.18 Chandigarh, India 0.42 (rural) and 0.35 (urban). Dublin, Ireland 0.22, Honolulu, Hawaii 0.16 Moscow, Russia 0.28. Nagasaki, Japan 0.21. Nottingham, UK 0.22 (Sartorius et al, 1986)

5.5.3.3 Riyadh districts

The distribution of schizophrenia cases did not follow a specific pattern, however it shows high rates in the *South* "Al-Hayer (0.000375); Al- Shfa (0.000242); Al-Azezyah (0.000237)", *East* "Al-Naseem (0.000261); Al-Rodah (0.000261)" *Central* Al-Shmesi (0.000222)", and also the north area of the city "Al-Shmal (0.000292)". Some of these areas are poor with high population density. The west area had the lowest schizophrenia cases and this area is considered to be a high-class residential areas but the north area, which showed high rates, is also considered to be a high class residential area as well.

This study shows high rates for schizophrenic male cases in poor central / areas in Riyadh which is in line with previous studies (Hare, 1956 a b) but the highest rates of schizophrenic female cases occurred in what is considered to be a good north area. This may suggest that the social class distribution for females may be very different from that of males.

5.5.3.4 Immigrants

There has been an increasing number of papers supporting the increased rates of schizophrenia among immigrants in Britain (Harrison et al 1988; Wessely et al 1991; King et al. 1994; Van Os et al 1996), United States (Halpern, 1993 ; Rabkin, 1979; Murphy, 1965) and the Netherlands (Selten &Sijben, 1994; Selten et al, 1997) Sweden (Zolkowska et al, 2001). The current study results contrast these western countries studies as it shows that incidence of schizophrenia is higher for Saudis than non-Saudis (IRR 26.41; 95% CI 14.28- 48.84; p= 0.00). However,

this might not be reliable for a number of reasons. Some of the non – Western migrant workers share the same culture with the Saudi people and have the same attitude to traditional healing. Others who come from South East Asia are unlikely to attend Saudi traditional healers. Secondly, people from South East Asia usually come to work in low-paid jobs such as maids and drivers. Usually the domestic workers and drivers are taken to work in the country by agents and hence the employers do not take responsibility for their health conditions. Any worker who starts showing signs of mental illness is quickly deported back to their native country. This quick deportation reduces the number of immigrants presenting at hospitals with mental disorder. The employers are the ones who organize the deportation or demand that the agents do so. This might be one of the reasons that the incidence rate of schizophrenia among immigrants is so low compared to immigrants to other nations in Europe and Africa (Samer & Yamout, 2012).

On the other hand, it is worth mentioning that Saudi Arabia unlike other western nations has very strict immigration rules and often refuses immigrants entrance to their country. What these strict immigration rules have done is to reduce number of immigrants in the country by a large number and hence the few that are there will be more selected and this might also reduce the immigrants' incidence of schizophrenia (Sonmez et al, 2011).

There is a large number of Saudis who do not care or even bother with the health of the immigrants even if it is their own worker. It is possible that when the worker who is an immigrant falls ill, the employer might simply ignore the

sickness or the symptoms of the sickness as long as the worker performs their work. When the symptoms worsen the employer will order their deportation. (Hannawi & Salmi, 2013).

5.5.3.5 Age

Differences in age of onset overlap with gender differences in schizophrenia (Goldstein et al, 1989). Men usually develop the illness at an earlier age than women. However, one study found that male and female have similar age distribution regarding early-onset (Castle et al, 1998). On the other hand the differences in age of onset appear can be explained on the presence or absence of family history, with no differences being found between men and women if they had a family history (Albus et al, 1994). The result of this study confirms that schizophrenia incidence is higher among the young population.

5.5.3.6 Gender

Gender differences in incidence have been found in different age groups (Räsänen, 1999). The number of females among later-onset schizophrenia patients on a par with the number of males among earlier-onset cases therefore results in an overall equal sex ratio of incidence rates (Castle et al. 1995). These findings have been confirmed in Jablensky et al study (1992). On the other hand, some studies suggested that the incidence of schizophrenia might be higher in males rather than in females such as Iacono & Beiser study (1992). Their study examined all first-episode cases of psychosis from a catchment area of 480 000 persons. Results showed that the annual incidence of schizophrenia in males (0.7 per 10 000) comparing to (0.2 per 10 000) for women. Higher annual incidence

rates of DSM-III-schizophrenia among men in Nottingham was also reported in Cooper et al study (1987) figures were (1.7 per 1026000) for men and (0.7 per 10 000) for women. It is important to mention that most of these studies did not include late-onset cases and thus this may be the reason for the difference in schizophrenia rates among gender. In developing countries, McGrath and co workers reported in their study that no significant gender differences have been found in schizophrenia incidence (McGrath et al, 2004). The gender differences in rates are more prominent with narrower definitions of schizophrenia. The study presented in this thesis found that schizophrenia incidence is higher among male than female using ICD 10 schizophrenia

5.5.3.7 Population density

In this study, schizophrenia incidence did not change as population density increased. This result is in contrast to previous findings (Laird, 1973; Paykel et al. 2000; Van Os et al, 2003; Sundquist et al. 2004; Weich et al. 2006; Dekker et al. 2008) However, it agrees to a certain extent with what Losert and co workers reported in their study, where results indicated that admission rates for schizophrenia increased as population density declined (Losert et al. 2012). It has been confirmed in number of studies that urbanicity is a risk factor for higher rates of schizophrenia incidence. Urbanicity is often defined as "high population density" (Sundquist et al. 2004; Dekker et al. 2008). However, this association between high population density and schizophrenia incidence high rates is non-linear association (Losert et al. 2012) in our study there was no effect of population density on the Saudi population incidence. This can be understood in a number of ways. Firstly low population density might be an

indicator of poor economic development which might be related to socio-economic disadvantage and therefore to an increase risk of mental disorder (Losert et al. 2012). However the Saudi results were adjusted for area income. Secondly, some studies underlined the possibility that people with psychological problems might experience a stronger feeling of social exclusion in small communities rather than large communities (Parr et al. 2004; Watkins & Jacoby, 2007; Thornicroft, 2008).

5.5.3.8 Marital status

The results of this study are consistent with previous studies which noted that psychosis rates are highest among widowed, divorced and separated groups, than among single group and the lowest rates are found among the married (Dunham, 1966; Turner et al, 1970). Another study reported that single males are 5.4 times greater to develop schizophrenia than married males (Malzberg, 1936).

5.5.3.9 Unemployment

There are number of studies that support the existence of an association between unemployment and increased rates of schizophrenia (Henderson et al, 1998; Zimmerman & Katon, 2005; Fortney et al, 2007,2009; Jia et al, 2009; Marwaha et al .2009; Boydell et al 2013), This Saudi study confirms this association but of course we cannot be sure of the direction of effect. Paul and Moser (2009) stated in their meta-analysis study, that the pressure caused by being unemployed might trigger mental illness.

5.6 Conclusion

My findings demonstrate associations between schizophrenia incidence and younger age and male gender. While unemployment is positively associated with higher rates of schizophrenia, area level income and population density were not associated with it. The study also highlights the association of single and divorced martial status with higher rates of schizophrenia in Saudi Arabia. The following chapter will provide the results from study II of this research "Factor analysis of schizophrenia symptoms and signs and their relation to demography in a Saudi sample"in a paper format, arranged into introduction, methods, results and discussion.

CHAPTER 6: FACTOR ANALYSIS OF SCHIZOPHRENIA SYMPTOMS AND SIGNS AND THEIR RELATION TO DEMOGRAPHY IN A SAUDI SAMPLE

6.1 OVERVIEW

Dimensional structures of psychosis have been examined in many studies mostly from Western countries, but have not been conducted in Arab countries before. The aim of this study is to describe symptom dimensions using detailed psychopathological information rated using the Operational Criteria Checklist for Psychotic Illnesses OCCPI from incident cases of schizophrenia, and then examine the associations of the symptom dimensions to demographic data and indices of premorbid risk. Factor analysis of OPCCI items from a total of 421 schizophrenia patients in Riyadh who presented between 2009 and 2011 was carried out. Associations between the five factors and demographic/pre-morbid data were then modelled using linear/logistic regressions. Results showed that factor analysis produced five-symptom dimensions: mania, depression, reality distortion, disorganisation, and manic /bizarre delusions explaining 33% of the total variance. Different dimensions were differentially associated with the demographic /premorbid risk factors. In other words, despite the cultural differences the dimensions are similar with what have been found in Western countries.

6.2 INTRODUCTION

Schizophrenia is a mental illness that exists across time, place, culture and religion. It has distinctive yet varying manifestations, and there have been many attempts over the years to classify the clinical features of this illness in order to better understand it (Cardno et al., 1996). Traditionally, symptoms are grouped according to a categorical classification such as the Diagnostic and Statistical manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) and the International Classification of Diseases (ICD-10) (World Health Organization, 1993). These categorical representations are advantageous in that they are familiar and easy to understand, as well as enabling a dichotomous decision making process. The inherent disadvantage of these classification systems is that they are not based on empirical investigations, but are rather a reflection of historical traditions. The validity of such an approach has been questioned due to the overlap between schizophrenia and other psychotic diagnoses in their premorbid risk factors, signs symptoms and treatment effects (Murray et al 2004; Allardyce et al. 2007). Therefore, a dimensional approach to psychiatric diagnoses was recommended by the APA and its partners in the International conference, which was held in July 2006 'The Future of Psychiatric Diagnosis: Refining the Research Agenda' (Regier, 2007).

The psychopathological dimensions were defined as "groups of symptoms which occur together more often than would be expected by chance alone" and this can be approached by using exploratory factor analysis (EFA) (Allardyce et al. 2007). The dimension system was derived from empirical research and numerous factor analysis investigations. Nevertheless, while the factor system allows for a more accurate portrayal of the patient's unique presenting symptoms, its focus is

more descriptive rather than diagnostic (Van Os et al., 2003). Thus, while the dimensional representation provides more information and does not impose categorical boundaries (often forcing the clinician to categorise the patient as 'atypical'), the number of dimensions and their essence remains controversial. On the other hand using both of categorical and dimensional systems has been advocated as a better strategy in conceiving psychotic illnesses (Demjaha et al, 2009).

For the past twenty years, OCCPI (Operational Criteria Checklist for Psychotic Illnesses) (McGuffin, Farmer and Harvey, 1991) has been used extensively as a reliable tool for characterising psychopathology. It consists of a 90-item checklist based on operational criteria for the major psychiatric classification systems. Though it is used for diagnosis, data derived from its application can be used to further analyse patients' symptoms (Brittain et al., 2013a). Correlations between the OPCRIT diagnosis and diagnosis using other classification systems are these clinical diagnoses were found to be moderate (Brittain et al., 2013b).

OPCRIT defines psychotic symptoms categorically or with a limited range. In addition, the OPCRIT includes a wide range of psychotic symptoms, mainly positive ones. Consequently, factor analyses have often involved the division of the positive symptoms into finer categories (Cardno et al., 1996).

So far, there is no final agreement as to the number of the symptoms dimensions of psychosis, however studies have suggested three or more factors (Liddle 1987; Murphy et al. 1994; Andreasen et al. 1995). Critics of the three-factor

model_ (positive, negative and disorganisation) state that it oversimplifies the presenting symptoms, and fails to provide useful insight as to a patient's prognosis and course of treatment (Mass et al., 2000). Though various studies have found specific associations between abnormal brain structures and the negative scale, as well as behavioural patterns consistent with the disorganised scale, a five factor model has been proposed to better reflect each patient's unique manifestation of the disease (Mclntosh et al., 2001; Peralta & Cuesta, 2001; Van Dael et al., 2006).

All studies have however been conducted in developed Western countries and its not known whether the dimensions described are universal or culture specific. The current study draws on a sample of 421 patients with schizophrenia seeking treatment in all six governmental hospitals in Riyadh, Saudi Arabia, and evaluates the five factor model and its ability to statistically distinguish unique and explanatory patterns. The age criteria was between 16 and 65 years old. The study received ethical approval from both King's College London, the Saudi Ministry of Health, and then ethical approval was obtained from each hospital included in the study.

6.3 METHODS

6.3.1 Sample

6.3.1.1 Catchment area

Riyadh is the capital of Saudi Arabia, It covers around (2000) square kilometers with a population around 5.7 million inhabitants. The city of Riyadh is served by number of Ministry of Health (MOH) hospitals, and other governmental hospitals, which provide psychiatric services. The hospitals included in this study were: The Amal Complex for Mental Health, King Abdulaziz Medical City

(KAMC), Prince Sultan Military Medical City (PSMMC), King Saud Medical City (KSMC), King Faisal Specialist Hospital & Research Centre (KFSH&RC), King Khalid University Hospital (KKUH).

6.3.1.2 Patient identification

Case ascertainment has been previously mentioned in details in the methodology chapter. We identified cases by generating a list of all patients from computer records in each hospital included in the study from 2009. ICD-10 codes of F20-F29, and from F30-F32 (World Health Organization, 1992) were used to identify possible cases. Only true incident cases were included in this study (i.e. had never contacted psychiatric services previously for psychosis) over a period of 2 years (2009-2011). Non-Saudis patients were excluded from this study as were those who were not resident in Riyadh city, had contacted psychiatric services previously, or had an organic psychosis.

6.3.2 Assessment of psychopathology

6.3.2.1 Symptom ratings

Information was extracted from patient's medical files. All cases were rated by myself only and therefore inter-rater reliability was not relevant. I was trained in the use of the instrument by my first supervisor, Jane Boydell. OPCRIT is a 90-item checklist for psychotic and affective symptoms. It is widely used as a polydiagnostic assessment tool with a good reliability and validity (Craddock et al., 1996;Azevedo et al., 1999).

6.3.2.2 Statistical analysis

Statistical analyses were performed using SAS (version 9.3; SAS Inc. Cary, NC, USA). All tests were 2-tailed with an alpha level of 0.05.

I. Selection of symptoms for entry into factor analysis

16 patient history items were excluded from the total 90 items leading to74 OPCRIT items. Following Allardyce et al (2007) "Irrelevant items to phenomenology were excluded, or where it would be difficult to determine if they were primary or in fact, secondary to medication (initial/middle insomnia, excessive sleep, reduced concentration, slowed activity, loss of energy, increased appetite, weight gain/loss)"

Afterwards, items that didn't have enough variability or that could lead to unstable factor analysis calculations were excluded as well (Allardyce et al 2007). Finally, the remaining 51 OPCRIT items were entered into factor analysis (see Table 6.1).

II. Exploratory factor analysis

Exploratory factor analysis (EFA) was chosen for this study to explore the underlying dimensions rather than testing previous developed model. Among the 51 OPCRIT items, some were 3 or 4 scale ordinal items and others were binary items. We initially ran analysis for three through six factors based on previous studies (Demjaha et al, 2009) and decided upon the five-factor solution as it had very good interpretability of the factors. In addition, we inspected the factor solution by the "eigenvalue greater than 1" rule, and the scree plot to guide the number of factors to include in the model.

These were subjected to oblique (promax, correlated) rotation to find a solution with the best simple structure, that is, a pattern of results such that each variable loads highly onto one and only one factor. In other words, only items with robust loadings of greater than 0.4 were used (Dikeos et al, 2006; Demjaha et al, 2009). Regression factor scores were then calculated based on the factor loadings of that rotation.

III. The relationship of dimensions to known demographic/premorbid risk factors

After we determined the number of factors, we fitted a series of linear/logistic regression models (controlled for age and gender), with the dimensional scores as the independent variables and each demographic/pre-morbid factors as the dependent variable: gender, age at onset, marital status, unemployment at onset, poor pre-morbid social adjustment, premorbid personality disorder, alcohol and drug abuse within one year of onset of symptoms, a definite psychosocial stressor prior to onset, family history of schizophrenia, family history of other psychosis, poor work adjustment, and coarse brain disease prior to onset.

6.4 RESULTS

6.4.1 Patient characteristics

This study used information gathered from the hospitals in Riyadh during the years 2009-2011. The OPCRIT questionnaire was completed from the case notes of 426 patients. Among these we included the 421 patients in the study who had the age of onset with 16-65 years old. Of these, 293 were male (69%) and 128 were female (31%). Mean age of onset for disease was 27 years and median age of onset was 26. 131 of the participants were married (31%), and 290 were

single (69%). In addition, 266 subjects were employed at onset of disease (63%) and 155 were unemployed (37%). The vast majority of patients (80%) experienced a gradual or insidious onset spanning six months or more, with 162 patients (38.5%) experiencing a premorbid personality disorder, and 390 (92.6%) experiencing poor premorbid social adjustment. As defined in OPCRIT. Only 57 patients (13.5%) had a family history of schizophrenia, though 156 (37%) had a family history of other psychiatric disorders. The vast majority of patients (98.6%) experienced poor work adjustment. Only 63 patients (15%) had abused alcohol or drugs within the past year, only 3 patients (0.7%) had coarse brain disease prior to onset, and 85 patients (20%) had definite psychosocial stressor prior to onset.

6.4.2 Factor structure

There were 17 factors with eigenvalues greater than 1; the scree test suggested an 8-factor solution, while a 5-factor solution was selected here in order to increase the parsimony of the model and as a 5-factor solution was associated with superior interpretability of the factors. A Promax rotated solution was used, with these results presented in Table 6.1.

Figure 6.1 Scree test

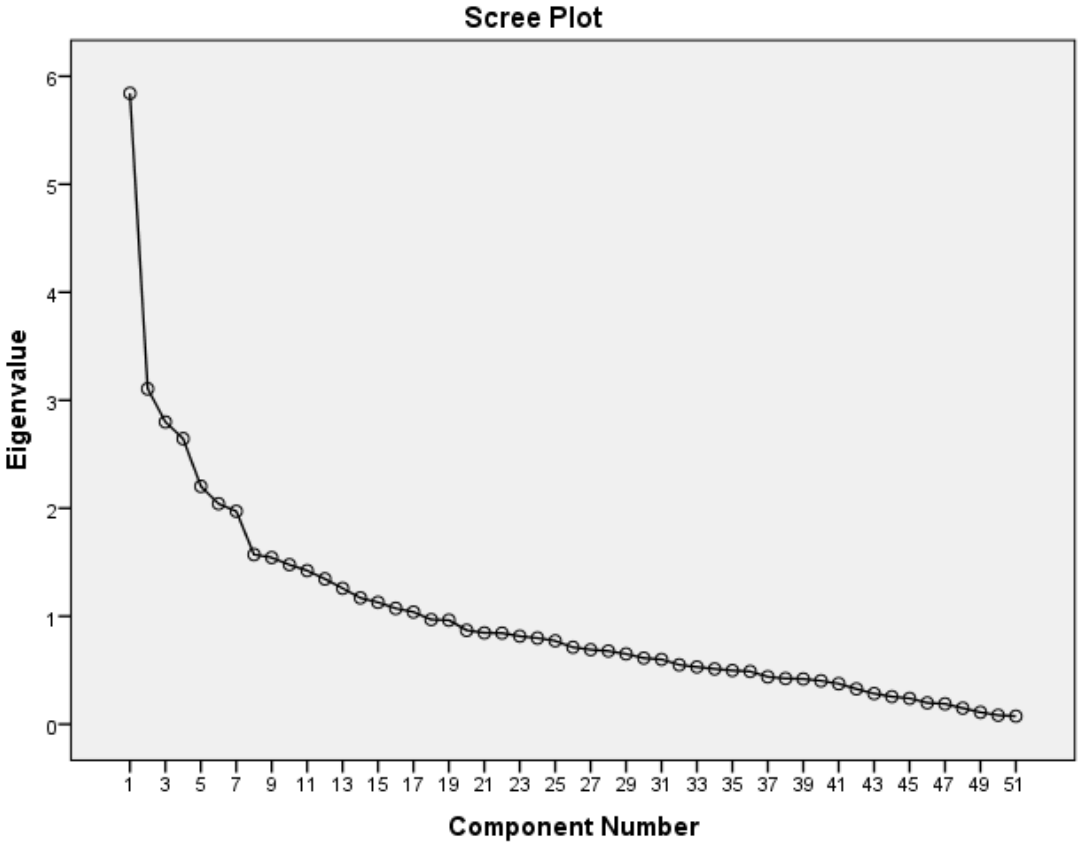


Table 6.1: Five-Factor Solution, Promax Rotation

	Factor				
Item	1	2	3	4	5
Factor 1: Mania (11.5%)					
Excessive activity	**.683**	-.148	-.078	061	.143
Reckless activity	**.622**	.004	.029	.113	.171
Slowed activity	**.719**	.219	.125	.008	-.125
Loss of energy/tiredness	**.678**	.268	.144	.013	-.152
Restricted affect	**.487**	-.097	.006	.038	.314
Elevated mood	**.613**	-.036	.152	.059	-.330
Irritable mood	**.662**	.066	.198	.054	-.269
Factor 2: Depression (6.1%)					
Dysphoria	.025	**.813**	-.027	.007	-.028
Loss of pleasure	-.035	**.848**	-.014	.010	.134
Excessive self-reproach	-.118	**.720**	.055	.122	.000
Suicidal ideation	.171	**.749**	.023	.085	.086
Factor 3: Reality Distortion (5.5%)					
Delusions of influence	.168	-.093	**.537**	-.173	-.014
Delusions of passivity	-.039	.010	**.600**	.196	-.048
Thought insertion	-.021	-.032	**.763**	.138	-.004
Thought withdrawal	-.029	.078	**.807**	-.034	.187
Thought broadcast	-.003	.086	**.774**	-.064	.203
Abusive/accusatory/persecutory voices	.209	.026	**.459**	-.062	.008
Factor 4: Disorganization (5.2%)					
Speech difficult to understand	-.042	-.142	.160	**.445**	.187
Positive formal thought disorder	.076	.056	.016	**.844**	-.041
Pressured speech	.037	.103	-.015	**.871**	-.060
Thoughts racing	-.020	.031	-.033	**.864**	-.084
Factor 5: Manic/Bizarre Delusions (4.3%)					
Bizarre Behaviour	-.062	-.320	.031	.135	**.418**
Increased self-esteem	.213	.042	.054	-.081	**.419**
Grandiose delusions	.227	.076	.025	-.084	**.479**
Bizarre delusions	.058	.205	-.154	-.046	**.625**
Primary delusional perception	-.020	.196	-.223	.007	**.560**

Based upon the results of this analysis, factor 1 was found to focus upon mania, with factor 2 focusing upon depression, factor 3 focusing upon reality distortion, factor 4 focusing upon disorganisation, and factor 5 focusing upon manic/bizarre delusions.

6.4.3 Association of dimensions to known demographic/premorbid risk factors

The following table (6.2) summarizes the results of the regression models conducted. Logistic regression was used in all models with the exception of the analysis conducted with the age of onset, which used linear regression.

First, factor 1 "manic" was found to significantly associated with being single (OR=724, *P*<. 05), alcohol/drug abuse (OR=1.531, *P*<. 05) and psychosocial stressors prior to onset (OR=792, *P*<. 05). Following this, factor 2 "depression" was not associated with any of the demographic /premorbid risk factors. Factor 3 "reality distortion" was found to significantly associated with both poor premorbid social adjustment (OR=1.641, *P*<. 05) and premorbid personality disorder (OR=733, *P*<. 01). Next, factor 4 "disorganization" is strongly associated with both unemployment (OR=1.312, P<. 01) and family history of schizophrenia (OR=1.339, *P*<. 05), while factor 5 "Delusions" associated significantly with being single (OR= 1.683, *P*<. 001), Unemployed (OR= 1.660, *P*<. 001), poor premorbid social adjustment (OR= 645, *P*<. 05,), premorbid personality disorder (OR= 1.520, *P*<. 001) and family history of other psychiatric disorders (OR=750, *P*<. 01).

No significant predictors were found with regard to poor work adjustment or coarse brain disease prior to onset.

Table 6. 2 Regression Analyses

Demographic/premorbid risk factors	*F1*	*F2*	*F3*	*F4*	*F5*	*Age*	*Gender*	*Constant*
Gender [a]	1.030	.938	.969	1.398**	.893	1.044***	–	.119***
Age of Onset [b]	-.388	.602	-.268	-.753	.118	–	2.218*	29.100***
Single at presentation [b]	724*	.866	1.054	1.198	1.683***	.845***	.192***	370.484***
Unemployed [b]	.844	.958	.943	1.312**	1.660***	.986	.669	1.255
Poor morbid social adjustment	1.288	.800	1.641*	1.938	.645*	1.031	.816	7.867**
Premorbid personality disorder [b]	1.059	.958	.733**	1.099	1.520***	.996	.525**	.836
Alcohol/drug abuse [b]	1.531*	1.100	1.140	1.274	1.296	1.023	.157***	.117***
Definite psychosocial stressor prior to onset [b]	.792*	1.184	1.131	.992	1.041	.990	1.601	.283**
Family history of schizophrenia [b]	1.229	.973	1.205	1.339*	.980	1.015	1.143	.089***
Family history of psychosis [b]	1.094	.973	1.125	1.118	.750**	.997	1.076	.599
Poor work adjustment [b]	1.113	.648	.934	4.024	.735	1.082	1.519	12.692
Brain disease [b]	631	.138	.196	2.758	.547	1.057	.000	.000*

Note. *p<.05, **p<.01, ***p<.001; [a]Odds Ratios; [b]Unstandardized Coefficients.

6.5 Discussion

6.5.1 Finding

This study shows a symptom structure composed of 5 dimensions: Mania, depression, reality distortion, disorganisation, and manic/bizarre delusions, which explain 33% of the variance. Symptom dimensions showed different associations with demographic data and pre-morbid risk factors.

6.5.2 Methodological consideration

- The amount of variance explained by the five-factor solution in this study (33%) is low comparing with previous studies.
- In terms of data validity, the researcher identified symptoms and risk factors from the hospitals medical record. Any errors would be likely to be random.
- Inter-rater reliability, inter-rater agreement, or concordance is the degree of agreement among raters. Since this study had only one rater, inter-rater reliability for OPCRIT couldn't be demonstrated, but of course wasn't needed.

6.5.3 Symptoms dimension

The results of our study are consistent with previous studies, however, there are some differences. In terms of the number of factors, the five factors model is supported in the literature. Some studies have produced the following dimensions: negative, positive, excitement, cognitive, and depression/anxiety (Lindström et al, 1993; Lindenmayer et al ,1994). In Dikeos et al. research (2006), which was based on psychosis patients, five factors were distinguished

(mania, reality distortion, depression, disorganization, negative symptoms); however, all were more variable in schizophrenia than in affective psychosis. Mania was the best discriminator between schizophrenia and affective psychosis; the negative symptom factor included blunted affect, negative formal thought disorder, restricted affect and slowed activity. Another study examined the relationship between the symptom dimensions and outcome in schizophrenic patients. The sample consisted of first-episode patients (n=156) and chronic patients (n=1571). The five dimensions that were found in the first-episode sample were: negative, delusional, depressive, manic grandiosity and hallucinations while the five dimensions that were found in the chronic patients were: negative, positive, depressive, hostile and disorganization (Salokangas, 2003).

The existence of two dimensions "manic" and "depression" containing affective symptoms have been mentioned in previous studies, some of which were about patients with psychosis (Mclntosh et al., 2001; Serretti et al., 2001; Dikeos et al., 2006; Allardyce et al., 2007) but other studies were only restricted to schizophrenia patients (Hutchinson et al., 2007; MacCabe et al., 2002 ; Salokangas et al., 2003; McGrath et al., 2004; Kopelowicz et al., 2008). Mania and depression may also be correlated with the dimensions of excitement and depression/anxiety described in other studies (Kay& Sevy, 1990; Lindenmayer et al., 1994). The clustering of mania and depression as independent factors suggest that affective symptoms are integral the schizophrenia process as defined by this set of criteria (Shergill et al., 1999) .

"Disorganization" dimension is also reported previously in schizophrenia patients (Grube et al., 1998) and in psychosis patients (Allardyce et al., 2007).

Our results did not produce a "negative symptoms dimension", which might be because we used OPCRIT, which is, as opposed to other diagnostic schedules, does not contain many symptoms affiliated with the negative category. It is important to say that some previous studies have managed to obtain a negative symptom dimension despite the use of OPCRIT alone (Cardno et al., 1996; Van Os et al., 1999; Dikeos et al., 2006). However, this can be also explained due to their study sample, which contains not only schizophrenia as this study but it included mood disorders with psychosis, schizoaffective disorder and other psychotic illnesses (Van Os et al., 1999; Dikeos et al., 2006) or because they used mixed stage/chronic samples where negative symptoms have a higher prevalence (Cardno et al., 1996).

Not all studies preduced a single positive symptom dimension . In some studies , the analysis broke down the positive dimension into two or more subdimensions (e.g., first rank delusions, paranoid delusions, first rank hallucinations, other hallucinationns) especially amongst broad psychosis samples (Toomy et al., 1997; Van Os et al., 1997; Cardno et al., 2001: Alardyce et al., 2007) and among schizophrenia/schizoaffective samples (Cardno et al., 1996, 1997; Lastra et al., 1996) .One explanation might be that this is due to the duration of untreated psychosis (DUP) as the median DUP of this sample was 1.41 years (interquartile range (IQR) 0.35-2.81 years) (see chapter 7 for more details), and according to some studies, longer DUP is associated with poorer outcome in terms of positive symptoms (Boonstra et al , 2012).

6.5.4 The association of dimensions to known pre-morbid risk factors

No previous studies (based on schizophrenia samples) - to the best of our knowledge - addressed the association of dimensions to known pre-morbid risk factors. The only studies we can compare are those based on psychosis sample.

In addition to the present study, Allardyce and others study (2007) has also found that different dimensions were associated differentially with the pre-morbid risk factors

Contrary to previous studies (Dikeos et al., 2006; Allardyce et al, 2007), our dimensional model showed a significant association between gender and disorganization factor, but no association have been found between any dimension and age at presentation in this study which is consistent with the Dikeos et al (2006) study but contrary to the Allardyce et al (2007) study, which indicated a significant association between age of onset with disorganization, depressive and delusional dimensions.

Some associations between the five dimensions and the demographic/premorbid risk factors have been found in this study. Significant results were found for all predictors included in the regression models with the exception of factor 2 "depression", which have been reported previously in the Dikeos et al (2006) study.

In terms of unemployment, our study shows a significant association with disorganisation dimension, which was also presented in the Allardyce et al (2007) study.

Nevertheless, the genetic contribution to the disorganisation dimension that was indicated by Rietkerk and colleagues (2008) was also present in the current sample, as

our results showed that family history of schizophrenia was associated with the disorganization dimension. In terms of "family history of other psychosis", this was found to be associated with the manic/bizarre delusions dimension in this study. This result is not consistent with previous findings that showed no or only a weak association (Allardyce et al., 2007; Mclntosh et al., 2001; Gardno et al., 1996).

6.6 CONCLUSION

The factor analyses in the present study produced a five-factor model, explaining 33% of the total variance. Different dimensions were differentially associated with the demographic /premorbid risk factors. The five-factor model has been proposed to better reflect each individual appearance of the illness. The five-factor model in an Arabic country is fairly similar to that found in Western countries, adding to the validity of the approach. The following chapter will provide the results from study III of this research "Duration of Untreated Psychosis and Pathway to Care in Riyadh, Saudi Arabia" in a paper format, arranged into introduction, methods, results and discussion.

CHAPTER 7: SUDY III - DURATION OF UNTREATED PSYCHOSIS AND PATHWAY TO CARE IN RIYADH, SAUDI ARABIA[1]

7.1 OVWERVIEW

Recent studies of 'duration of untreated psychosis' (DUP) indicate that some patients remain untreated in the community for some time. Considerable emphasis has been placed on reducing the DUP. However, most studies investigating DUP have been conducted in Western countries, where well-developed primary care systems are available. The key objective of this chapter is to describe DUP and its association with both demographic factors and pathways to care in Riyadh, Saudi Arabia. A retrospective study of 421 new case records of all Saudi schizophrenia patients over a 2-year period in six governmental hospitals in Riyadh, Saudi Arabia was used. Results showed that the median DUP was 1.41 years (interquartile range (IQR) 0.35-2.81 years). The longest time to contact was 9.86 years but 90 % had a DUP shorter than 5 years. Older age at onset, single marital status and higher educational levels were associated with shorter DUP. Long DUP was associated with help seeking from traditional healers. In conclusion, in Saudi Arabia, it usually takes longer for patients to seek help from psychiatric services after their first psychosis onset

[1] N.B chapter adapted from: Alfayez, H, Lappin, J, Murry,R, Boydell,J. 2015. Duration of Untreated Psychosis and Pathway to Care in Riyadh, Saudi Arabia. *Early Intervention in Psychiatry* Online ISSN: 1751-7893 (see appendix 4)

than it does in Western countries. The results suggest that the DUP is influenced by both demographic factors and pathways to care.

7.2 INTRODUCTION

The difference between the time that patients present for psychiatric care and the time that they had their first episode of schizophrenia is termed 'duration of untreated psychosis' (DUP). Studies of DUP have indicated that some patients remain untreated in the community for 1-2 years (McGlashan, 1999; Barnes et al, 2000; Ho et al, 2000). More recent studies have indicated a shorter DUP: 44.6 weeks (Malla et al., 2002) 18.6 weeks (Rosen and Garety, 2005) 11 weeks (Morgan et al., 2006). This later study was based in UK cities. Most studies have been conducted in in Western countries, where well-developed primary care systems are available. It is unclear how generalizable such findings may be to countries with less developed psychiatric services, and few studies to date have been conducted in developing countries.

One such study that compared DUP, in Egyptian and Saudi patients, with first - episode psychosis, explored the socio-demographic, clinical and help-seeking characteristics between the two samples. The mean DUP did not significantly differ (3.2 years Egyptian; 3.1years Saudis) (Fawzi et al, 2011).

Sharifi and co-workers conducted a study of first-episode psychosis (FEP) in patients in Iran and, unexpectedly, found that the median DUP was 11 weeks, thus comparable to that found in Western studies. Similar proportions of patients initially sought help from psychiatrists (n = 23, 25.3%) as from traditional healers (n = 21, 23.1%), with a smaller proportion seeking help first from a general practitioner (n = 16, 17.6%) (Sharifi et al, 2009).

Causal attributions, pathway to care and clinical features were examined in a sample of 54 first-episode psychosis patients in South Africa to test if there were associations between these factors and DUP. The results showed that both spiritual attributions of cause (49% of patients) and a previous consultation with a traditional healer (39% of patients) were associated with long DUP (Burns et al, 2011). Another study was conducted in Karachi, Pakistan (Naqvi et al, 2009), and showed that because of the lack of a primary care system, most of the psychotic patients contacted psychiatrists directly. Understanding the importance of early diagnosis and treatment is an important step to eliminate this delay and mitigate its impact on the prognosis of the disease. The first stage of help seeking is the decision to seek help and this is what seems to be prone to most delay (Jones et al, 1993; McGorry et al, 1996). The decision is influenced by a large amount of factors, perhaps the most important of which are cultural (Vogel et al, 2007). In Saudi society, the delay that occurs before seeking help could be potentially understood as due to the belief that supernatural powers such as magic are the cause of these symptoms (Al-Subaie & Alhamad, 2000).

The main aim of this study is to describe the duration of untreated psychosis in the capital city of Saudi Arabia. The secondary aim is to identify any associations between DUP and both patient demographic factors (nationality, age, gender, income, marital status, living status (i.e. living with family, living alone and other), family size, education level, employment status, monthly income, history of drug abuse) and their first pathway to care (non-psychiatric and psychiatric health profession– traditional healer/other religious person).

7.3 METHODS

A descriptive and analytical study utilising retrospective evaluation of 421 new cases of schizophrenia patients records (in and out patients) from all governmental hospitals in Riyadh, Saudi Arabia. The city of Riyadh is served by number of Ministry of Health (MOH) hospitals, and other governmental hospitals that provide psychiatric services. Hospitals included in this study were: The Amal Complex for Mental Health, King Abdulaziz Medical City (KAMC), Prince Sultan Military Medical City (PSMMC), King Saud Medical City (KSMC), King Faisal Specialist Hospital & Research Centre (KFSH&RC), and King Khalid University Hospital (KKUH). This provided comprehensive coverage of all inpatients and almost all outpatients undergoing treatment for psychosis in Riyadh. Inclusion criteria were as follows: all schizophrenic patients who did not have an organic psychotic illness (based on ICD-10 (10^{th} revision of the International Statistical Classification of Diseases and Related Health Problem)), age at onset from 16 up to 65 years, residents of Riyadh city, no previous contact with any psychiatric services and Saudi nationality. The age range was chosen to reflect clinical practice. From a total of 425 patients satisfying the inclusion criteria, 4 patients were excluded due to poor quality information, giving a total sample of n = 421. There were neither dropouts nor censorings due to the nature of the study design. Among the 421 patients, 211 records had date of onset given by day and 210 patients had date of onset given by month so an approximated date of 1^{st} of each month was substituted. Therefore, the maximum discrepancy from a true value could have been 0.083 year (=30 days). For the endpoint, all records recorded the day.

Ethical approval for this study was granted from both Kings College London and from the Institutional Review Board (IRB) of the Ministry of Health (MOH) Saudi Arabia. Approval to undertake this study and collect full demographic and diagnostic data from patients' medical files was also granted from all of the hospitals included in the study.

7.3.1 Sample

Clinical and demographic data on all people from Riyadh city, who presented with schizophrenia between 2009 and 2011, were collected. We identified cases by generating a list of all patients from computer records in each hospital included in the study from 2009. ICD-10 codes F20-F29, and F30-F32 (World Health Organization, 1992) were used to initially identify cases. Demographic factors and pathway to care were collected from patient records (nationality, age, gender, income, marital status, living status (i.e. living with family, living alone and others), family size, education level, employment status, monthly income, history of drug abuse and the treatment –seeking behaviours).

7.3.2 Diagnostic procedure

Only true incident cases were included in this study (had never contacted psychiatric services anywhere), and then all case notes were rated using the Operational Criteria (OPCRIT) checklist by the main researcher to determine ICD-10 schizophrenia diagnoses using the associated computer program.

7.3.3 Duration of untreated psychosis

Information was extracted from all the psychiatric records in order to verify the date of the onset of symptoms and treatment, pathway to care and socio-demographic variables. Onset of psychosis was defined as the presence for 1

week or more of one of the following psychotic symptoms: delusions; hallucinations; thought disorder; and bizarre, grossly inappropriate and/or disorganised behaviour with a noticeable deterioration in function. Following previous studies (Graig et al., 2000; Morgan et al., 2006), the endpoint of DUP in this study was considered as the date of first contact with mental health services whether they were admitted to hospital or only treated as outpatients.

7.3.4 Statistical Analysis

Comparisons between groups in the sample were conducted using the chi-squared test and the Wilcoxon rank-sum test, as appropriate for the distribution of the data. The DUP was defined as the period in days from the onset of positive psychotic symptoms until the start of psychiatric treatment. As noted in several other studies and also for our sample, the DUP did not have a normal distribution and was heavily skewed. Even after log transformation, the distribution still showed non-normality. This and the observation that DUP is time to event data led to the choice of survival analysis as the best approach to analyse the relationship between DUP and other variables. The onset of psychosis as defined earlier was chosen as the entry point and contact with services was the endpoint. Specifically, tests for univariable associations between DUP and other variables were carried out using Kaplan–Meier survival curves. Log-rank tests and Wilcoxon tests were performed to assess differences between groups in the survival probability. The Wilcoxon rank-sum test was also conducted to compare DUP between groups. A *p-value cut-off* point of 0.25 was chosen to select variables to be examined in a Cox proportional hazard regression. A high *P*-value was chosen to avoid missing any potentially important

variables in the multivariable model. For the purpose of statistical significance however, *P*-values of <0.05 were chosen. The final model with the smallest AICc (second-order Akaike Information Criterion) was chosen as the smaller AICc indicates the better model among a set of Cox regression models. Unadjusted and adjusted hazard ratios (HRs) of predictors included in the final model are presented.

The assumption of proportional hazards was found not to be invalidated in the final model. An HR >1.0 represents an increased risk of contact with services and hence indicates a shorter DUP.

All analyses were conducted using SAS (version 9.2; SAS Inc. Cary, NC, USA). All tests were 2-tailed.

7.4 RESULTS

7.4.1 Patient characteristics

Table 7.1 shows the social and clinical characteristics of the sample. Across the whole sample, the median DUP was 1.41 years (interquartile range (IQR) 0.35-2.81 years). The longest time to contact was 9.86 years but 90 % had DUP shorter than 5 years. The average age at onset in the full sample was 27.2 years (standard deviation (SD) =7.8) while the average age at contact was 28.9 years (SD=7.9). The sample was predominantly male (70%), of single/separated/divorced/widowed marital status (69%), of school education and lower (80%), of monthly income less than 8000 SR (60%), of no employment (63%), of 1-8 family members (60%), of living with family (91%).

Only 40% had first contact through a health professional (non-psychiatric and psychiatric), 83% had schizophrenia and only 18% reported drug abuse.

Table 7.1 Patient Social and Clinical Characteristics

Total Sample (n=421)			
DUP[1] in Years			
Mean(SD)[2]		1.89 (1.86)	
Median(IQR)[3]		1.41 (0.35-2.81)	
Age at Onset			
Mean(SD)		27.2 (7.8)	
Median(IQR)		26 (22-30)	
Age at Contact			
Mean(SD)		28.9 (7.9)	
Median(IQR)		28 (23-32)	
Gender		N	%
Female		128	30.51
Male		293	69.49
Social Status		N	%
Married		131	31.23
Single and Other[4]		290	68.77
Education		N	%
School or lower		332	79.90
University or Higher		84	20.10
	N Missing = 5		
Monthly Income		N	%
8000 SR or higher		167	40.0
lower than 8000 S		251	60.0
	N Missing = 3		
Employment		N	%
No		266	63.20
Yes		155	36.80
Family Size		N	%
1-8 members		253	60.49
More than 8		165	39.51
	N Missing = 3		
Living Status		N	%
Alone or Other[5]		36	8.52
With family		383	91.48
	N Missing = 2		
Pathway To Care		N	%
Non-Psychiatric and Psychiatric Health Profession		167	39.81
Traditional Healer and Other[6]		253	60.19
	N Missing = 1		
Drug Abuse		N	%
No		347	82.32
Yes		74	17.68

[1] DUP: Duration of Untreated Psychosis

[2] SD: Standard Deviation

[3] IQR: interquartile range

[4] "Single and Other" includes Single, Divorced, Separated, and Widow

[5] "Alone and Other" includes Alone, Prison, Social Institution and other

[6] "Traditional Healer and Other" includes Traditional Healer, Religious Person.

7.4.2 Univariable Associations between DUP and socio-demographic variables

To investigate the association between DUP and the categorical variables, a Wilcoxon rank-sum test was conducted and results are shown in Table 7.2. Single marital status, higher education and higher monthly income show strong associations (statistically significant at the $P < 0.05$ level) with shorter DUP. Pathway to care (i.e. consulting a traditional healer) showed a strong and statistically significant (at the $P< 0.05$ level) association with longer DUP. For the continuous variable, age at onset, the Pearson correlation coefficient was -0.12 (a low negative association), between age at onset and Log (DUP) with a *P*-value of 0.013.

Table 7.2 Wilcoxon rank-sum test results showing factors predicting DUP

Predictor	P-value
Gender	0.44
Social Status	0.02
Education	0.002
Monthly Income	0.02
Family Size	0.21
Employment	0.88
Living Status	0.75
Pathway to Care	<.0001
Drug Abuse	0.70

7.4.3 Univariable analysis using Kaplan-Meier curves, Log-Rank tests, and Wilcoxon tests

The association between DUP and other variables (except age at onset) were further investigated through Kaplan-Meier curves with log-rank and Wilcoxon tests. Table 7.3 shows that social status, education, pathway to care are associated with DUP and had *P*-values < 0.05. Monthly income and family size

are weakly associated with DUP. Monthly income had a *P*-value of < 0.05 but family size had a *P*-value of 0.21; this was therefore included in the multivariable model but was not a statistically significant univariable association. The Kaplan-Meier survival curves in Figs 7.1, 7.2 and 7.3 show a clear divergence in the survival probability (here the event is the contact to services) according to social status, education, and pathway to care. It is notable that the groups of single and other, of university or higher education and of initial pathway to care through health professional have a shorter DUP than their counterparts.

There was no evidence of an association between DUP and any of the other variables considered: gender, employment, living status and drug abuse. Thus these were not included in the multivariable Cox regression analysis

Table 7.3 Log-Rank test and Wilcoxon Test

Variables	Log-Rank Test			Wilcoxon Test		
	χ^2	DF	P value	χ^2	DF	P value
Gender	0.4	1	0.53	0.59	1	0.44
Social Status	10.12	1	0.002	5.37	1	0.02
Education	14.94	1	0.0001	10.44	1	0.001
Monthly Income	3.62	1	0.06	5.78	1	0.02
Employment	0.19	1	0.66	0.02	1	0.88
Family Size	2.8	1	0.09	1.56	1	0.21
Living Status	0.17	1	0.68	0.12	1	0.73
Pathway To Care	23.2	1	<.0001	17.77	1	<.0001
Drug Abuse	0.02	1	0.89	0.14	1	0.71

Fig 7.1 Survival curves for DUP, stratified by Social Status

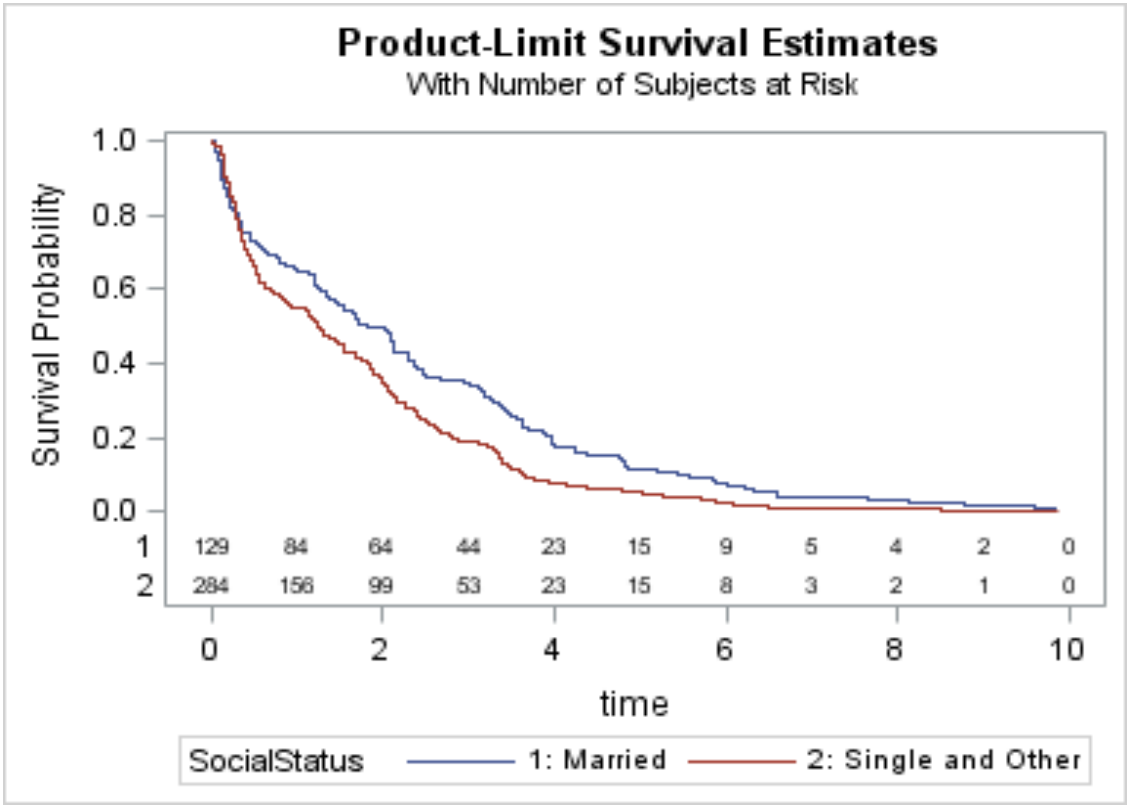


Fig 7.2 Survival curves for DUP, stratified by Education

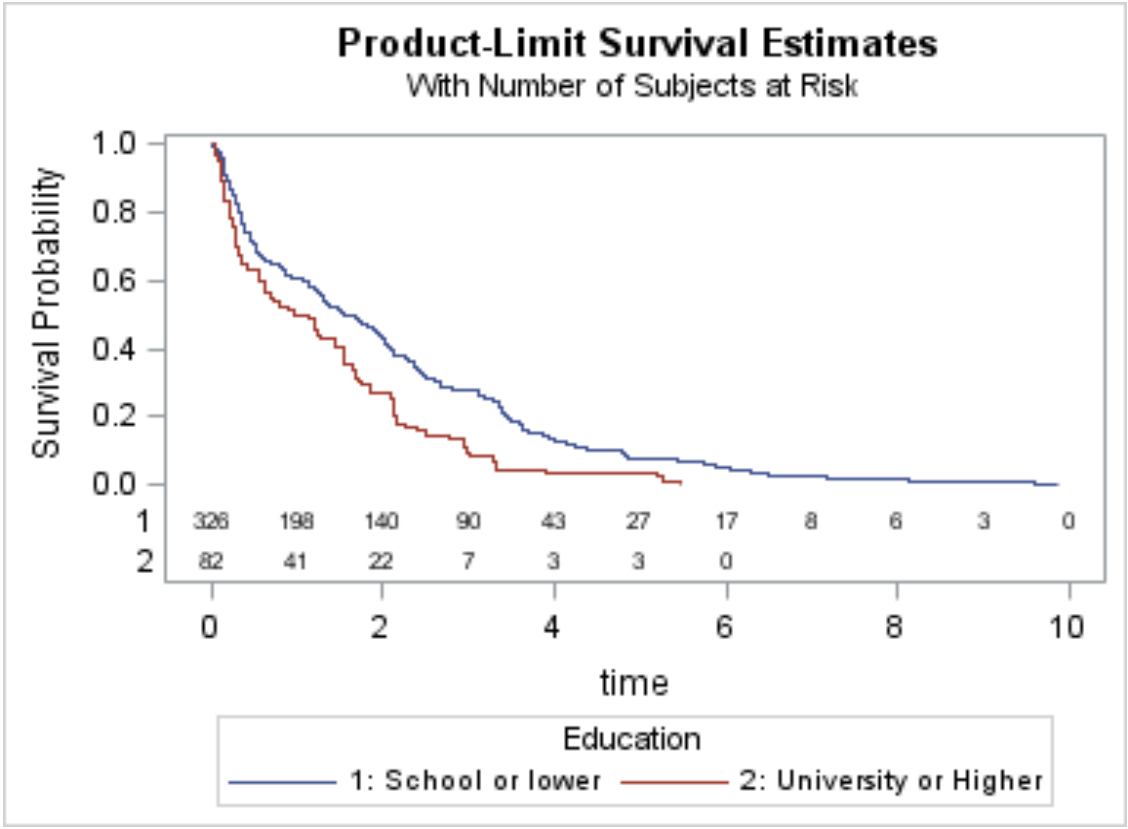
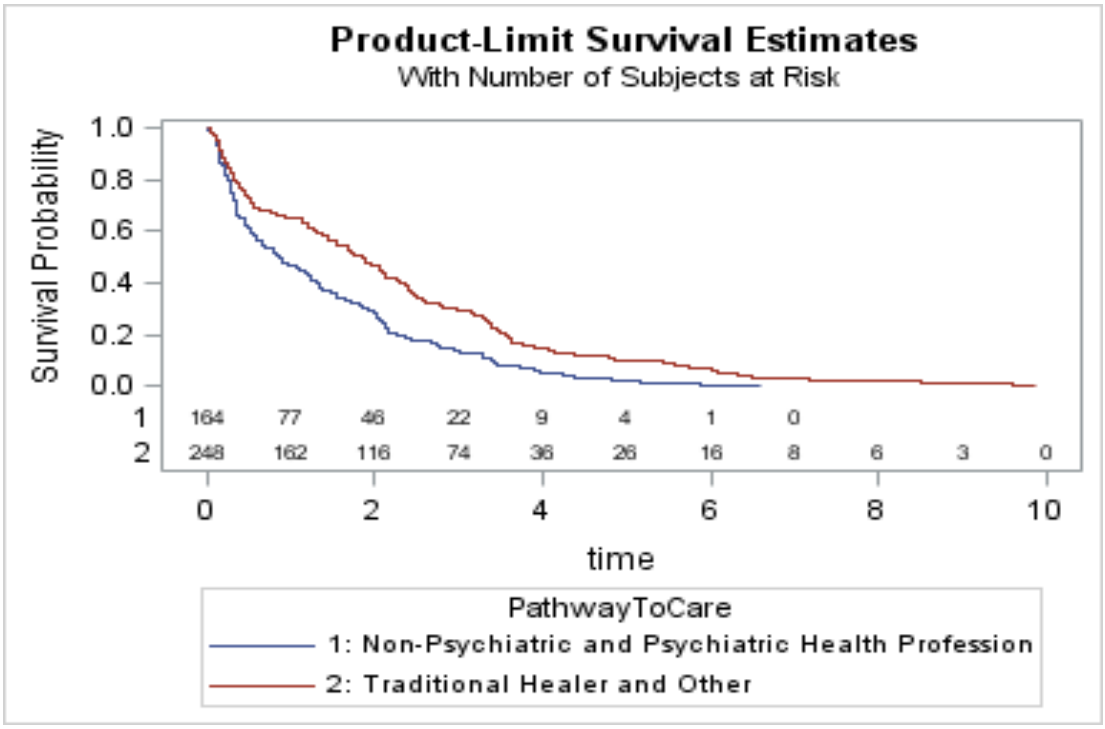


Fig 7.3 Survival curves for DUP, stratified by Pathway to care



7.4.4 Multivariable Results: Cox Proportional Hazards Regression

As above, a univariate Cox regression was performed for the following variables: age at onset, social status, education, pathway to care, monthly income, and family size. All of their *P*-values were smaller than the chosen cut-off *P*-value of 0.2525 for entry into the multivariable model. Among them, social status, education and pathway to care were statistically significant (*P*-value <0.05), so were included in the multivariate model first. Then, the model AICc was compared after adding/eliminating age at onset, monthly income, and family size. The final model with the smallest AICc had the predictors of age at onset, social status, education and pathway to care. Monthly income and family size were dropped in the final model somewhat expectedly since there was collinearity between social status and family size and between education and monthly income. The unadjusted and adjusted HR and corresponding 95 % CI, *P*-values are shown in Table 7.4. All of the four predictors included in the final model are strongly associated with DUP. The adjusted HR=1.02 for age at onset indicates that, overall, every year older at onset increases the risk of contact with services by 2% per year. After adjusting for other confounders, married status decreases the risk of contact by 33% within a year compared with single or other. After adjusting, education of school leaving level or lower decreases the risk of contact within a year by 31% compared with people with university or higher education. On the contrary, after adjusting, the pathway to care of initial contact with a Health Profession increases the risk of contact within a year by 69% compared with the pathway to care by traditional healer and other. Thus, older age at onset, single marital status and higher educational level were

associated with shorter DUP. Long DUP was associated with help seeking from traditional healers.

Table 7.4 Unadjusted and adjusted hazard ratios for DUP[1]

Predictor	Unadjusted HR	(95% CI)	P value	Adjusted HR	(95% CI)	P value
Age at Onset (per year)	1.01	(1.00, 1.03)	0.063	1.02	(1.01, 1.04)	0.002
Social Status						
Married vs Single or Other	0.71	(0.58, 0.88)	0.002	0.67	(0.54, 0.84)	0.0004
Education						
School or lower vs University or Higher	0.62	(0.48, 0.79)	0.0001	0.69	(0.54,0.89)	0.004
Pathway To Care						
Non-Psychiatric and Psychiatric Health Profession vs Traditional Healer and Other	1.64	(1.34, 2.01)	<.0001	1.69	(1.37, 2.08)	<.0001

[1] **Note:** The association of Monthly Income and Family Size with DUP in the Univariate Cox regression was also investigated. Unadjusted HR (95 % CI) and P value for Monthly Income (8000 SR or higher vs lower than 8000 SR) were 1.19 (0.97,1.45) and 0.09, and for Family Size (1-8 members vs More than 8) were 0.88 (0.72, 1.08) and 0.21.

7.5 DISCUSSION

7.5.1 Summary of results

This study is one of the largest investigations of DUP and associated variables in the Arabic world. It was conducted in all governmental hospitals to cover the whole area of Riyadh. The DUP was associated with certain demographic factors, that is age, marital status and education level. It was also associated with help seeking from traditional healers. Other factors including nationality, gender, income, living status, family size, employment status, monthly income and history of drug abuse were not predictive.

7.5.2 Methodological issues

7.5.2.1 Methodological weaknesses

As the study is retrospective, the available information was extracted from case records; this method is in line with previous studies such as Primavera et al (2012) and Thomas and Nandhra study (2009). A study by Morgan et al (2006) was conducted to test the clinical and social determinants of DUP. In that study, key information data were available for part of the sample from interview with patients and relatives in addition to the case records (66.3%); however, for the other part of the sample, the only available information was extracted from the medical records (33.7%). A comparison between the two parts of the sample was carried out testing for differences in age, gender, living circumstances, social status, education, employment, mode of onset and diagnosis and there was no evidence of any systematic information bias in that DUP could be established for both samples (Morgan et al, 2006).

It would have been very interesting and informative to test the factors that influenced time to help seeking from traditional healers but unfortunately the date of first seeing a traditional healer was not generally recorded so this was not possible in this study.

Similarly a detailed examination of severity and DUP would be useful, particularly investigating change in severity during the time without treatment.

7.5.2.2 Methodological strengths

Unlike many studies, this study included not only admitted patients but also all patients who made contact with any mental health services even if not admitted within the time frame of the study, which reduced selection bias. Private hospitals only provide outpatient services in Riyadh for psychiatry. They were contacted for the purpose of this study. Unfortunately, they did not allow access to patient files to collect data. However, they indicated that most schizophrenia cases are not new, that they have been seen before in governmental hospitals or clinics. We are therefore reasonably confident that coverage was as complete as possible. In addition, diagnostic objectivity was maximized by using Operational Criteria (OPCRIT) checklist and associated computer diagnoses.

7.5.3 Comparisons with previous studies

7.5.3.1 Median DUP

We found that the median DUP of patients from Riyadh was 1.41 years (interquartile range (IQR) 0.35-2.81 years), which is shorter than that reported by Fawzi et al (2011) in their study (3.2 years and 3.1 years for the Egyptian and Saudi patients, respectively). The reason for this may be the end of DUP

definition that we have adopted in our study, that is, any contact with services, whereas Fawzi defined the end of the DUP as 'the time of receiving first adequate treatment'; this might have given a shorter DUP median in our study. However, the median in our study is very long compared with those recently reported from western countries. Archie et al (2010) reported a median DUP of 22 weeks . Drake et al (2000) reported that the median DUP was 12 weeks. On the contrary, our findings are similar to other western studies from one to decades ago that reported that the median DUP was 1-2 years (McGlashan, 1999; Barnes et al, 2000; Ho et al, 2000).

7.5.3.2 Age

In this study wherein 421 psychiatric records of patients were verified and analyzed, it appears that the most frequent DUP is less than 5 years (90%), The longest time to contact was 9.86 years. Adjusted HR=1.02 for age at onset indicates that overall every year older at onset increases the risk of contact with services by 2% which mean a shorter DUP and this is consistent with Dominguez et al (2013) study which showed that adolescents had a longer DUP (179 days) than adults (81 days). The delays in identifying psychosis among adolescents can be understandable for a number of reasons. Firstly, some families consider psychosis symptoms as part of teenage behaviors or just a reaction to pressures and stress which might lead adolescents to be referred to teachers or social services rather than seeking help from a psychiatrist (Dominguez et al., 2013). Secondly, adolescent psychosis usually presents with a slow and insidious onset therefore, early recognition of the disorder can be very difficult (Rosen et al., 2006; Hollis, 2000). Thirdly, teenagers may be more

hesitant to see psychiatrists, therefore delaying diagnosis and treatment of the disease (de Haan et al., 2004). Other studies showed no association between DUP and age (Shrivastava et al, 2010; Drake et al, 2000).

7.5.3.3 Help provider

Patients who sought psychiatric help from mental health professionals or other medically trained professionals are more likely to have a shorter DUP. On the other hand, those who sought help from traditional healers first appear to have longer DUP. It sometimes takes five to ten years to treat the illness medically after an initial approach to traditional healers (n=59) than through a health professional (n=5). The findings show that seeking help first from traditional healers is more common in our sample (60%) compared to seeking help from a health professionals (40%). This is consistent with previous findings that showed that the traditional healer was the most frequent help-seeking first contact in both Egyptian and Saudis samples (Fawzi et al 2011). Other studies from developing countries showed similar results such as Chilale et al in Mzuzu (2014) (n=140), 60% of the patients sought help from traditional healers while only 28% sought help from hospitals. Burns et al (2011) showed that a longer DUP is associated with spiritual attribution and seeking help from traditional healers.

Saudi society tends to explain the sudden disturbed behaviour that appears in a person to be the result of witchcraft, evil eye, and demonic possession rather than scientifically explained as 'mental illness'. Jinn (demons), Sihr (magic) and Al-Ein or Nafs (evil eye) are all mentioned in the Holy Qur'an and that explains why they are mostly accepted in society (Al-Subaie & Al-Hamad, 2000). As a

result of these beliefs, the recognition of mental illness can be delayed which has been claimed to affect the disease progress and treatment (El-Islam,2008) .

It is important to point out that traditional healing is a legal major health system in Saudi Arabia. About 50% to 70 % of psychiatric outpatients have sought help from a traditional healer at some point of their illness; 21% to 50% did that before even being seen by a psychiatrist (Hussein, 1989; Al-Subaie, 1994). In an early study, about 60% of psychotic outpatients had been to a traditional healer before seeking help from a psychiatrist (Okasha et al, 1968). This is in contrast to studies from western countries, where the largest number of patients usually contact a physician first (Anderson &Malla, 2010).

A pilot study was conducted with 45 male traditional healers in Saudi Arabia to describe the narrated symptom pattern (psychological, physical and other symptoms caused by supernatural entities) and treatments given by them. The study revealed that traditional healers couldn't distinguish psychiatric symptoms and consider them to be symptoms of jinn possession, evil eye, and magic. This misunderstanding is due to the lack of awareness of psychotic illnesses and their symptoms, signs and treatment. (Al-Habeeb, 2003)

Traditional healers have a vital role in the early diagnosis of psychosis as many patients seek help from them before seeking any medical help. Therefore, It may be helpful if psychiatrists offer some training sessions, education and workshops for traditional healers in order to help them better understand and distinguish the psychosis symptoms and signs. This will help reducing the time wasted before seeking professional help.

7.5.3.4 Gender

In terms of gender, there were more men (n=287) than women (n=126) in this study and gender was not significantly associated with DUP. Previous studies have had mixed findings. Køster et al (2008) showed that women had a longer DUP. However several studies have shown evidence of a longer DUP in males (Fawzi et al, 2011; Larsen et al, 1996 ; Thorup et al , 2007). Both Shrivastava et al (2010) and Drake et al (2000) did not find an association between gender and DUP. A systematic review was conducted to assess the influence of gender on DUP, 27 studies (4721 patients) were included in this study. The results showed that no differences existed between the two genders with regard to DUP length (Cascio et al, 2012).

7.5.3.5 Marital status

Those who were married were more likely to have a longer DUP when compared to those who were single and other (divorced, separated, and widowed). This contrasts with Pek et al (2006) study, which showed that single patients had a longer DUP than married patients. However, other studies did not show any association between marital status and DUP (Craig et al, 2000; Naqvi et al, 2009). Our result might be understood by considering the impact of culture on making decision of seeking treatment. This might be influenced by lack of awareness of mental illness and stigma. The decision to seek treatment is often made by the family and not by the individual (Okasha, 2004), and if the patient is the wife, the husband is the one who decides whether to seek treatment or not as he has authority in Arab families (Morsy, 1993; Shalhoub-Kevorkian, 1999). The negative impact of mental illness on the family affiliation to the community

and the feeling of shame may delay treatment seeking (Okasha, 2005). The husband may think it is good for the family to keep the wife's illness as a secret in order not to affect their reputations in the society, which could affect the marriage of their children.

7.5.3.6 Educational level

Chen et al (2005) said that educational level is an important tool for early detection of psychosis. This study shows a higher DUP patients in 'school education and lower' category than for 'university education and higher'. However, it is not clear if being unable to finish standard level of education leads to a long DUP or long DUP increases school withdrawal and affects function negatively.

7.6 IMPLICATIONS AND LIMITATIONS

7.6.1 Implications

- People in Arabic countries, who are developing psychosis for the first time, have a longer duration of untreated psychosis than people in Western countries.
- It might be possible to educate Arabic society about the important role of psychiatrists and the services they provide and this might reduce the stigma of mental illness. This, in turn, might reduce the duration of untreated psychosis.

7.6.2 Limitations

- The number of cases is limited, and the results are based on the 421 psychiatric records.

- In terms of data validity, the researcher relied upon the data retrieved from the hospitals records.
- The study is focused on only one area, which is Riyadh, the capital of Saudi Arabia and one specific time, therefore the findings may not apply to other areas.

7.7 CONCLUSION

Although taking into account the limitations of the study, DUP tends to be long in Saudi Arabia, which is a major clinical concern. Seeking help from a traditional healer was a significant predictor of a long DUP. Younger age, married status and lower education level were the only demographic factors associated with a longer DUP. This chapter descried the duration of untreated psychosis in Saudi Arabia and examined its association with both demographic factors and pathway to care. The next chapter will provide the general discussion for the whole thesis in general.

CHAPTER 8: FINAL DISCUSSION AND CONCLUSION

8.1 INTRODUCTION

This chapter starts with a brief summary of the results. Next, the limitations of the research are presented and discussed in detail. After that the, results are interpreted in the context of the limitations and general conclusions are made. Finally this chapter proposes directions for future research

8.2 SUMMARY OF FINDINGS

8.2.1 Study I showed that the Incidence rate of schizophrenia was significantly different between Riyadh districts and it varied widely from 0 to 37.1 per 100 000 persons-years. In addition, the incidence rate of schizophrenia was higher within the younger population group. It was also higher for Saudi than non-Saudi people, for male than female and among unemployed rather than employed. Regarding the Saudi population, incidence of schizophrenia was higher within the younger population group as well. It was also higher for male than female and among unemployed rather than employed. There was no effect of population density. Regarding marital status, the results showed that the incidence of schizophrenia was highest among divorced and separated people and higher amongst single compared to married people. The area incidence of schizophrenia did not significantly differ by the monthly income level of the area.

8.2.2. Study II showed a symptom structure composed of 5 dimensions; mania, depression, reality distortion, disorganisation, and manic /bizarre delusions which explains 33% of the total variance. Symptom dimensions showed different association with known demographic /pre-morbid risk factors.

8.2.3 Study III demonstrated that the median DUP was 1.41 years (interquartile range (IQR) 0.35-2.81 years). The longest time to contact was 9.86 years but 90 % of patients had a DUP shorter than 5 years. Older age at onset, single marital status and higher educational level were associated with a shorter DUP. Longer DUP was associated with help seeking from traditional healers.

8.3 METHODOLOGICAL CONSIDERATIONS

Although this thesis consists of three studies, I will discuss the methodological considerations in general with the main focus on the epidemiological study, as this was the basis for the thesis. However as mentioned previously, the limitations of each study have also been discussed separately in the relevant results chapter.

Incidence studies and particularly comparisons of incidence across time or place are filled with methodological pitfalls as succinctly summarised by Kendell et al 1993, with particular reference to schizophrenia.

(a) Some people with schizophrenia may never seek medical care.

(b) Some people with schizophrenia who seek medical care may not be referred to psychiatrists.

(c) Some of the people with schizophrenia referred to psychiatrists as an outpatient and may never be an inpatient.

(d) If a percentage of people with schizophrenia move from one area to another before their illness becomes evident and these migration patterns change, the number of hospital first admissions from any given geographical area may change in the absence of any change in incidence.

(e) If the average age at which people with schizophrenia are first admitted to hospital rises over a period of time, the first-admission rate will fall over that time period, and vice versa.

(f) If there are significant variances in the incidence of schizophrenia in different social classes or ethnic groups and the class or ethnic composition of the population changes, the incidence of schizophrenia in that population will change.

(g) Not all schizophrenia patients are diagnosed at the time of their first hospital admission. Those in whom the diagnosis is made only at a second or subsequent admission will never appear in the first-admission statistics, and if the proportion of diagnoses delayed in this way (for valid or invalid reasons) changes the first-admission rate will change. Conversely, some of the patients diagnosed with schizophrenia on first admission will subsequently receive other diagnoses.

(h) If admission rates are expressed relative to the total population (i.e. per 100000 population), changes in the proportion of that population in the age range at risk of developing schizophrenia (say 144years) may either generate spurious changes in incidence or conceal genuine changes.

(i) In most case registers some of the patients recorded as first admissions are readmissions, either because the patient has concealed, or no one has enquired about, an earlier admission elsewhere.

(j) Diagnostic criteria may change in subtle ways during the study period.

In this research, I have tried to ensure the accuracy and validity of the study by ensuring that:

- The population at risk is large enough, stable geographically and statistically well characterised to provide accurate data on nationality, gender, age, and income for the denominator. Statistical procedures were carried out to standardise the results to allow comparison across areas.

- The study sample comprised all the new schizophrenia cases who presented to government secondary services during the study period; however some cases might have been missed out if they did not seek treatment through one of the government hospitals in Riyadh.

- The study sample contained the main age-of- risk range for schizophrenia.

- The study includes patients who made contact as well as all psychiatric contacts.

- The notes were checked to ensure the cases were true incident cases, but if this was inaccurate then a case might have been misclassified

- Diagnostic objectivity was maximised by using OPCRIT

8.3.1 Treated incidence as a proxy for incidence

One of the limitations of the research is the use of treated incidence as a proxy for true incidence. This could be inaccurate, as reviewing of patient files gives information about those who visited the hospitals or clinics so anyone who did not visit a clinic or hospital would not be included in this study. Unlike the European and American model of community care all psychiatric contacts occur in a hospital setting but some of these are as outpatients. Every attempt was made to include these contacts as well however some might have been missed if they first presented to one of the few private psychiatric clinics. These clinics were contacted and very low numbers were confirmed but I cannot say exactly how many might have been missed. No admissions could have occurred outside the governmental hospitals, as the private clinics do not have inpatient services.

The likelihood of missing community resident people who meet the diagnostic criteria for schizophrenia is an inevitable disadvantage of a retrospective secondary care based study design. Reasons for the choice of this design will be discussed below. European studies (Prince et al 1994, Geddes et al 1995) compared a community survey with a register study and demonstrated that almost all schizophrenia cases came into contact with secondary services. The research presented in this thesis is based in a very different culture and it is not possible to be sure whether contact rates would vary from Europe or in which direction. The culture of Saudi people being embedded in strong extended families might increase contact rates but stigma might reduce them. Different

considerations apply to non-Saudi people living in Saudi as they might be repatriated rather than present. This issue will be discussed in a later section.

8.3.2 Choice of Study Design

Incidence studies are useful for identifying patterns of disease, changes over time and place particularly, for service planning and for testing for associations. Treated incidence studies are practical for a severe disease with a low incidence such as schizophrenia. The alternatives to a treated incidence study are a cohort study or a community survey but they both have methodological and practical problems. A cohort study would be extremely expensive and would be subject to attrition bias. A community survey would be expensive, time consuming and subject to case ascertainment bias. These would not necessarily have any greater validity than a treated incidence study.

Kendell et al 1993 carried out a study to investigate and assess the influence of the factors he listed above to decide whether or not the incidence of schizophrenia was falling in the city of Edinburgh between 1971and 1989, using a well maintained case register covering the patient population whose case records were available for study. All the analyses that have been performed with these Edinburgh data produced a declining inception rate for schizophrenia between 1971 and 1989. Whether or not out-patients are added to first admissions, whether or not patients first diagnosed as schizophrenia during non-first admissions are included, and whether these “delayed-diagnosis” patients are attributed to their year of first admission or to their year of

diagnosis, the fall in the inception rate over the 19 years was always at least 25% and always statistically significant. On the other hand, this study has revealed two sources of bias that were at least exaggerating and probably creating the observed fall in the inception rate for schizophrenia. The first was changing diagnostic criteria. The second bias revealed here was the extent to which patients with previous admissions are wrongly coded as first admissions, even when the responsible clinician was aware of the previous admission. The study concluded this point could not be explored or assessed with data from a case register. However, Kendell also concluded that in industrial countries, almost all people with schizophrenia come to psychiatric attention sooner or later, and this assumption is supported by the results from population surveys.

Since this foundation work, the problems of both under ascertainment and case ascertainment selection bias have been addressed to some extent in the literature by other epidemiologists. Prince and Phelan (1994) established that there are almost no people with schizophrenia known to GPs in South London who have not been in contact with psychiatric services. Geddes and Kendell (1995) concurred and also demonstrated that almost all patients treated as outpatients were admitted at least once during their lifetime.

Some studies even questioned the feasibility of administrative data. The aim of Goldacre et al (1994) was to estimate the incidence and prevalence of treated schizophrenia by analysing patient records in Oxfordshire who contacted psychiatric services during 1975-1986. The results of this study showed that even though "first admission rates" for schizophrenia are useful indicators of the

general pattern of disease they are inadequate as absolute indicators of the true incidence. The research conducted for this thesis and most recent studies made a point to include contacts as well as admissions. Vanasse et al (2012) noted in his study that incidence of schizophrenia can be estimated using administrative data. These estimates appeared to be a valid step toward appropriate planning of services for schizophrenia illustrating the usefulness of the data despite the possibility of missed cases.

There are many published studies that have used treated incidence as a proxy for true incidence including the highly respected, classic work of Mortensen et al (1999). For example, Anderson & Hynnekleiv (2007) calculated the incidence rates of treated cases of psychosis and suicide in historical cohorts of a small rural community in southeast Norway and compared the local findings with the national ones. Only patient records who were born in the rural community after 1845 who had contacted the mental hospitals were reviewed. The results showed that the overall local incidence rates of psychosis and suicide seem to be representative for the country at large suggesting substantial underestimation is unlikely or at least consistent. One of the most recent studies following up attenuated psychotic symptoms in Israel used service level outcome data as a proxy for true incidence (Webeloff et al 2012). They discussed the issue of non-presentation and attempted some follow-up of the cohort in person reporting that 93% of those with schizophrenia were hospitalized at some time.

Although the use of treated incidence as a proxy for true incidence has difficulties these appear (at least in the West) to be more theoretical than real.

Studies described above that have directly addressed it have been reassuring. Much valuable work has been done using treated incidence as a proxy for true incidence that has then been replicated by different groups in different countries with different social circumstances. This methodological concern cannot be easily overcome, leaving a choice between abandoning incidence work or continuing whilst thinking about the likely direction and extent of any underestimation or case ascertainment bias. The consensus seems to be that the value of incidence work is such that it should continue as evidenced by recently published studies. This problem is not unique to psychiatry and valuable research has been conducted using imperfect incidence estimates in HIV, cancer and cardiovascular epidemiology. The alternative of psychiatric evaluation of a population is usually not feasible due to funding constraints and the approach of large-scale surveys using questionnaires can also miss cases and be misleading.

8.3.3 Accuracy and standardisation of Diagnostic Procedures

This study involved rating a wide range of case records to include any possible psychosis to standardise the diagnostic procedure and minimise diagnostic bias. This is an improvement on the use of routine statistics. Some studies have evaluated the use of routine statistics (without further diagnostic clarification) to estimate true incidence but diagnostic consistency is generally preferred (Van Os et al., 2000). Reliable, standardised diagnoses were made by the OPCRIT computer programme. One advantage of the OPCRIT system is that different diagnostic systems can be used. ICD-10 diagnostic criteria were used for this thesis. This requires that symptoms last for one month so these rates will be

higher than if DSM IV was used (this requires six months duration) and lower than if RDC criteria were used (two weeks).

8.3.4 Government hospitals vs. Private hospitals

The second limitation of this study is that only government hospitals were included in the study. There are no private psychiatric in-patient facilities in Riyadh, ensuring that all psychiatric admission are represented in the study. Private hospitals were contacted for the purpose of this study. Unfortunately, they did not allow access to patient files to collect the data. However, they indicated that most schizophrenia cases are not new, that they have been seen before in government hospitals or clinics. It should be noted that military hospitals are government hospitals.

It is important to note that currently psychiatric care is provided by a number of psychiatric and general hospitals and clinics (MOH, 2009). In Riyadh, recently a high proportion of general hospitals have established psychiatric wards, including King Faisal Specialist Hospital, the Military Hospitals, the Central Hospital, and King Khalid Hospital. Services are not sector based, as in the UK, so a person can attend any hospital. Because of the concentration of hospitals and services within Riyadh it is unlikely people who live in the capital city would seek care outside the capital city. Access to care can be self-referral, family facilitated or by the police. Compulsory treatment does occur in accordance with Saudi law. Concerned employers can arrange for assessment of sick employees.

Health services including medication are provided free, not only by MOH but also by other government sectors. All, but the private hospitals, are fully funded by the government. This might be a reason for people to seek treatment through one of the government hospitals in Riyadh especially as schizophrenia medicines are known to be costly. Furthermore, due to the nature of schizophrenia, the disorder requires that the individual takes medications for long periods which might cause a financial burden to the patients, so they are more likely to seek treatment from government hospitals rather than private. Hence, I am fairly confident that I did not miss a large number of cases.

One final point worth mentioning is that the most highly qualified doctors, whom people prefer to go to because of their good reputation, are working in government hospitals and not in private hospitals.

8.3.5 Gender Differences in Access to Care

There are differences in access to care particularly for women (Saudi or migrant) in Saudi Arabia, as they are dependent upon men to take them to appointments or to be admitted. However, social conditions are rapidly changing, and travel by women in taxis (called by women themselves) and with private drivers, especially in the capital city, is becoming more common. Statistics estimated that the number of private drivers reached approximately 800,000 in Saudi Arabia (CDSI, 2013). Mental health services are freely available for women as above. There is therefore a potential problem with under ascertainment in women, but there is no reason why it would be differential by

area or social class. It was thought likely that women would present later but this was not the case as demonstrated by the Duration of Untreated Psychosis study.

8.3.6 Migrants Access to and Utilisation of Psychiatric Care

Even though the number of non-Saudis in Riyadh is around 1,500.000 only a very small number of schizophrenia incident cases were found, (14 cases) and the possibility of under ascertainment needs to be considered.

Most of the non – Western migrant workers share the same culture with the Saudi people and have the same attitude to traditional healing. Others who come from South East Asia are unlikely to attend Saudi traditional healers. Healthcare is available free of charge to migrant workers in Saudi. There is therefore no cultural reason why most migrants would not access care to a greater or lesser extent i.e. there should not be differential case ascertainment to any significant degree on the basis of access to care.

Recently, the number of Immigrant has increased in Saudi Arabia due to good and numerous job prospects in the oil and natural gas industries that require huge amounts of skilled manpower. Settling in Saudi Arabia for work has been increasing among the people from neighbouring countries.

The 2012 annual report for Amnesty International regarding Saudi Arabia said that foreign worker' rights are being violated on a large scale such as non-payment of salaries, poor living and working conditions and not having any

protection from the labor law in Saudi Arabia. Many foreigners, who are working as domestic workers, mostly women, are forced to stay in abusive conditions, where they are forced to work up to 18 hours a day for a pittance or, in some cases, without pay. A study was conducted in Saudi Arabia to highlight the demographic and clinical characteristics of 122 foreign patients' utilisation of psychiatric services. They included 40 male and 72 female with age-range 16-55 years. Mean age was 32.7 and 94 (84%) were working abroad for the first time. Mean duration of stay in the country was 41 months. Results showed that psychotic disorders were common among South East Asians while Mediterranean and African patients were more likely to be diagnosed with affective disorders. This study suggested that ethnicity affects the pattern of stress vulnerability and tolerability, but it was not a large or epidemiological sample. South East Asians frequently face social difficulties and are exposed to uncertain residency and legal status, which make them more vulnerable to stress. Thus, some migrants may develop adjustment or stress disorders shortly after coming to Saudi Arabia and others may develop psychotic or affective disorder if they stay for a longer duration (Lotaief et al 2009).

The very low number of cases in migrants was unexpected. Migration to Saudi is largely for work and there is likely to be selection effect in that migrants would be healthier. Social conditions can be very stressful for migrants however and this would be expected to increase the incidence. It is very possible that migrants who are becoming unwell would be returned to their country of origin. It is still difficult to understand that there were only 14 cases from a population at risk of 2.200.000 Psychosis can have a sudden onset but these cases might

have not have met the one month duration of symptoms criteria for ICD 10 schizophrenia. Furthermore it is possible that people who made contact with services were moved before one month expired. Unfortunately it was not possible to address these issues within the study. The study design was a retrospective case note study. It assumed that notes were kept. If the notes for migrant workers were destroyed or returned with the patient to their country of origin the rates would appear artificially low.

8.3.7 Denominator population

In the incidence study, the 2005 census was used to estimate the population denominator, as it is the last census available to us with all the variables under study. This is considered highly accurate in a well-regulated society. However, I recognize that the population at risk during the study period may differ a little, but there is no reason to suspect that I have introduced systematic bias by age, gender or social class. The migrant population has probably increased and this would bias the incidence to appear higher than it is in reality i.e. the opposite of my findings.

8.3.8 Individual-level risk factors

Not all individual-level risk factors were controlled for in the incidence, especially family history of psychosis, which could potentially explain a degree of clustering of risk in some neighbourhoods. However to reduce the effect of this problem I used incidence rather than prevalence data over a short study period. Social class at the individual level may have contributed to the variation that was been observed at the level of neighbourhoods, but could not be adjusted, as the information was not available. It was not possible to obtain

denominator data stratified by a fifth variable (Social class). Place of residence at onset of psychosis was measured in this study rather than at birth or during upbringing. This is relevant to any aetiological processes involving proximal social factors that this study aimed to investigate.

8.3.9 Neighbourhood-level variables

Ethnic densities were calculated from the 2005 census. It is important to note that this study was limited to "Saudis" and "non-Saudis," this is due to the lack of detailed information on the non-Saudis nationalities across neighbourhoods.

8.4 COMPARISON WITH PREVIOUS WESTERN FINDINGS

8.4.1 Study I

The effect of individual-level male gender and younger age, were in the expected direction (Van Os et al, 2000; Boydell et al, 2001) in addition to the effect of unemployment (Boydell et al, 2013) and being divorced (Van Os et al, 2000). This study showed higher incidence rate for men (70%) similar to 61% and 57% for men in both Van Os and Boydell studies respectively. The mean age for this study was younger (28 years) while it was (35.5) in Van Os study and (34.5) in Boydell study, probably reflecting the younger population.

This study confirms the effect of spatial and geographical variations in the distribution of schizophrenia. It shows that the incidence of schizophrenia varies between neighborhoods which is consistent with previous studies (Faris & Dunham 1939; Hare, 1956a/b; Van Os et al., 2000; Boydell et al., 2001) .The incidence rate in the current study varied widely from 0 to 37.1 per 100 000 persons-years comparing to Boydell's results (2001) (varied from12 to 38 per

100 000 persons-year), but less than Van Os's study (2000) (varied from 0 to 51 per 100 000 persons-year). On the other hand, comparing to the AESOP findings, the incidence rate recorded in this study is lower than the incidence rate in South-East London (55 per 100,000 person years) but higher than both Nottingham and Bristol (25 per 100,000 person years and 22 per 100,000 person years, respectively)(Morgan et al, 2006).

The results for the distribution of schizophrenia cases confirm those of previous studies (Faris and Dunham, 1939; Hare, 1956). There are, however some differences. As in Faris and Dunham's study, the central area of the city showed a high rate of schizophrenia, but this high rates occurred not only in the poor central area but also in the wealthy central area , which is similar to what Hare (1956) found. However, it was difficult for this study to point to a common social factor in both areas such as high population density or disorganisation as in Faris and Dunham's study or high proportion of persons living alone as in the Hare study (1956) and Van Os et al study (2000) or the effect of minority ethnic groups as in Boydell et al (2001) study. The results did not show any effect for population density on the incidence rate, opposite findings regarding minor ethnic effect on the incidence rate and it was impossible to study the effect of proportion of persons living alone due to the lack of relevant data.

The peripheral areas of a city are thought to have lower schizophrenia rates as in Faris and Dunham's study (1939), but this depends on the organisation of the particular city and distribution of putative risk factors. In Riyadh, similar to Hare's study(1956) the distribution was not so clear . Our findings showed that remote southern areas of the city showed high rates of schizophrenia whereas

the remote northwestern areas of the city did not.

In order to explain this distribution of schizophrenia in poor and wealthy central areas of Riyadh, a number of possibilities should be considered. Firstly, the free treatment under the MOH and the other governmental hospitals in Riyadh helped to reduce the differences between rich and poor people in their methods of seeking medical help.

Secondly, the internal migration and residential mobility of people might be important factors for this distribution (which has not been considered in the current study). A Saudi Study indicated that most of the first-generation internal migrants constitute 91.5% of the families in the center areas of Riyadh. Most of these internal migrants are coming from the South-West of Saudi Arabia (74.8 of households in central areas are coming from Jazan). The mean age of the internal migrant when he came to the city of Riyadh was young (28.6 years). Economic factors are the most important reasons for migration to Riyadh, whether looking for work (82.5%), or moving from inadequate public services (49%). This same study revealed that the main attractions for housing in central of Riyadh for immigrants are economic factors in the first place (low rent 53% - low house prices 13.3% - monthly installments for rent 11.6%) and social factors in term of the presence of relatives (35%) (Al-Nuaim, 2004). In developing countries, internal migration movement might have led to a rise in mental disorders. Also the accompanying economic and social changes might have led to the high rates of mental illness (Okasha, 2005).

8.4.2 Study II

Although our results are similar to previous western studies in terms of number of factors, there are some differences. The most important results of this study are, the presence of two dimensions of positive symptoms and the absence of a negative symptom dimension, although there were not many negative symptoms in the checklist. It should be noted that it might be difficult to make a clear and direct comparison with previous studies due to different collecting data methods, diagnostic criteria's and statistics. This was discussed more fully in Chapter 6.

8.4.3 Study III

It was not surprising that the median DUP in Riyadh is very long compared with those recently reported from western countries but on the other hand it was similar to older western studies. This longer DUP in Saudi patients appears to be explained by cultural beliefs, traditional healers, stigma and services.

8.5 INTEGRATING FINDINGS

This thesis has discussed schizophrenia in the capital city of Saudi Arabia from three different perspectives, but overall gives a clearer and more comprehensive picture than was previously available. The study confirms that the incidence rate of schizophrenia in Saudi Arabia is similar to those recorded in Western capitals. The incidence, standardized for age and gender varied from 0 – 37 per 100 000 persons-years in different neighborhoods and most of the cases are located in the central, south and east of the city. The effect of individual-level male gender, younger age, being unemployed and being divorced were all in the expected

direction. The Saudi schizophrenia patients showed a longer DUP (median 1.41 years / interquartile range (IQR) 0.35-2.81 years) compared to western countries with a five-symptom dimensional structure: mania, depression, reality distortion, disorganisation, and manic type delusions explaining 33% of the total variance.

8.6 IMPLICATION OF FINDINGS AND FUTURE WORK

The findings presented within this thesis provide evidence of substantial variation in the incidence of schizophrenia across areas in Riyadh, which cannot be accounted for by variation in population structure (age, sex, ethnicity) nor to the wealth of the area. It was very interesting and to my knowledge a unique finding that population density did not predict incidence.

The findings also suggested that, as in the West, schizophrenia is more commonly found among the younger generation with an increase in males. As in the West marital status and unemployment were found to be associated with incidence.

Despite the important role played by community mental health services for people with mental disorders, such services have not yet been established in Saudi Arabia (Al-Habeeb & Qureshi, 2010). This study showed the significant role played by religion and faith healers in the life of people with schizophrenia. Integration of these two systems would be likely to reduce the duration of untreated psychosis and might be of public health benefit.

Future work on the incidence of schizophrenia in Saudi Arabia could focus on exploring the differences in incidence rate between rural and urban areas in Saudi Arabia besides determining whether there is an urban rural difference or whether this is also not demonstrable. This would provide important clues as to the cause of the urban rural difference identified in the Western world.

8.7 CONCLUSION

The thesis has presented a comprehensive picture of the epidemiology of schizophrenia in the capital city of Saudi Arabia, duration of untreated psychosis and a factor analysis of symptoms of schizophrenia.

REFERENCES

Abdul Karim, M. Al Haddad, M.K. (1998). Incidence of schizophrenia at first admission in Bahrain. *Egyptian Journal of Psychiatry21, 95-100*

Abdul-Hamid, W. (2003). Introduction to the Psychiatry of Ancient Iraq. *Arab Journal Of Psychiatry*, *14*(2), 129.

Abiodun, O. A. (1995). Pathways to mental health care in Nigeria. *Psychiatric Services*,46(8),823-826

Abou-Saleh, M. T., Ghubash, R., & Daradkeh, T. K. (2001). Al Ain community psychiatric survey. I. Prevalence and socio-demographic correlates. *Social psychiatry and psychiatric epidemiology*, *36*(1), 20-28.

AbuMadini, M. S., & Rahim, S. I. (2002). Psychiatric admission in a general hospital. Patients profile and patterns of service utilization over a decade. *Saudi medical journal*, *23*(1), 44-50.

Addington, J., Van Mastrigt, S., & Addington, D. (2004). Duration of untreated psychosis: impact on 2-year outcome. *Psychological medicine*, *34*(02), 277-284.

Adeosun, I. I., Adegbohun, A. A., Adewumi, T. A., & Jeje, O. O. (2013). The pathways to the first contact with mental health services among patients with schizophrenia in Lagos, Nigeria. *Schizophrenia research and treatment*, *2013*.

Agara, A. J., & Makanjuola, A. B. (2006). Pattern and pathway of psychiatric presentation at the out-patient clinic of a neuro-psychiatric hospital in Nigeria. *Nigerian Journal of Psychiatry*, *4*(1), 30-34.

Albus, M., Scherer, J., Hueber, S., Lechleuthner, T., Kraus, G., Zausinger, S., & Burkes, S. (1994). The impact of familial loading on gender differences in age at onset of schizophrenia. *Acta Psychiatrica Scandinavica*, *89*(2), 132-134.

Aleman, A., Kahn, R. S., & Selten, J. P. (2003). Sex differences in the risk of schizophrenia: evidence from meta-analysis. *Archives Of General Psychiatry*, *60*(6), 565-571.

Al-Habeeb, A. A., & Qureshi, N. A. (2010). Mental and Social Health Atlas I in Saudi Arabia: 2007-08. *Eastern Mediterranean Health Journal*, *16*(5).

Al-Habeeb, T. A. (2003). A pilot study of faith healers' views on evil eye, jinn possession, and magic in the kingdom of Saudi Arabia. *Journal of family & community medicine*, *10*(3), 31.

Al-Issa, I. E. (2000). *Al-Junūn: Mental illness in the Islamic world*. International Universities Press, Inc.

Al-Krenawi, A., & Graham, J. R. (2000). Culturally sensitive social work practice with Arab clients in mental health settings. *Health & Social Work*, *25*(1), 9-22.

Allardyce, J., Gilmour, H., Atkinson, J., Rapson, T., Bishop, J., & McCreadie, R. G. (2005). Social fragmentation, deprivation and urbanicity: relation to first-admission rates for psychoses. *The British Journal of Psychiatry*, *187*(5), 401-406.

Allardyce, J., McCreadie, R. G., Morrison, G., & van Os, J. (2007). Do symptom dimensions or categorical diagnoses best discriminate between known risk factors for psychosis?. *Social Psychiatry And Psychiatric Epidemiology*, *42*(6), 429-437.

Al-nuaim, A. (2004). Urban Poverty and its relation to Internal Migration In Riyadh City

Al-Rabdi, M.S. (2004). Analysis of census results. Riyadh Newspaper, Economy Section,7 December.

Al-Shahri, M. Z. (2002). culturally sensitive caring for Saudi patients. *Journal of Transcultural Nursing*, *13*(2), 133-138.

Al-Shawi, M. (1998) Qur'anic treatment of the magic and Satanic Possession .dar alam alktab .Beirut.

Al-Subaie, A. (1990). Psychiatry in Saudi Arabia: an overview. *Psychiatric Bulletin*, *14*(5), 298-300.

Al-Subaie, A., & Al-Hamad, A. (2000) Psychiatry in Saudi Arabia. In: I Al-Issa, ed .Al-Junun: mental illness in the Islamic world. Madison, CT, International Universities Press, 205-233

American Psychiatric Association. (1994). Diagnostic And Statistical Manual Of Mental Disorders DSM-IV Author: American Psychiatric Association, Publisher: America.

Andersen, J. E., & Hynnekleiv, T. (2007). Hospital-treated psychosis and suicide in a rural community (1877–2005). Part 1: Incidence rates. *Acta Psychiatrica Scandinavica*, *116*(s436), 6-19.

Anderson, k. K., Fuhrer, R. & Mall, A. k. (2010). The pathways to mental health care of first-episode psychosis patients: a systematic review. *Psychological Medicine,* 40, (10), 1585–1597.

Andreasen, N & Black, D. (2000.). Introductory Textbook of Psychiatry (4th ed.). Washington, DC: American Psychiatric Publishing, Inc

Andreasen, N. (1979) Affective flattening and the criteria for schizophrenia. *The American Journal of Psychiatry*, *136*(7), 944-947.

Andreasen, N. (1984). Scale for the assessment of positive symptoms. *Iowa City: University of Iowa*.

Andreasen, N. (1995). Symptoms, signs, and diagnosis of schizophrenia. *The Lancet*, *346*(8973), 477-481.

Andreasen, N. (1997). Linking mind and brain in the study of mental illnesses: A project for a scientific psychopathology. *Science, 275*, 1586–1593.

Angermeyer, M. C., & Matschinger, H. (1996). Relatives' beliefs about the causes of schizophrenia. *Acta Psychiatrica Scandinavica*, *93*(3), 199-204.

Anglin, D., Stanford, A. D., Harkavy-Friedman, J. M., Goetz, R., Rosenfield, P., & Malaspina, D. (2009). Family history of affective illness in schizophrenia patients: Symptoms and cognition. *Schizophrenia research*, *110*(1), 24-27.

Archie S, AkhtarDanesh N, Norman R, Malla A, Roy P, Zipursky RB. (2010) Ethnic diversity and pathways to care for a first episode of psychosis in Ontario. *Schizophrenia Bulletin*, 36:688–701

Arehart-Treichel, J.(2003). Stress-Related Brain Changes Begin In Youth. Psychiatric News.38(22),26. American Psychiatric Association.

ArRiyadh Development Authority ADA (2011). High Commission for the Development of Arriyadh.

ArRiyadh Development Authority ADA (2013). High Commission for the Development of Arriyadh.

Avasthi, A., Khan, M., Elroey, A (1991) Inpatient sociodemographic and diagnostic study from a psychiatric hospital in Libya. *International Journal Of Social Psychiatry* 37(4), 267-279 (winter)

Aylward, E., Walker, E., & Bettes, B. (1984). Intelligence in schizophrenia: meta-analysis of the research. *Schizophrenia Bulletin*, *10*(3), 430-459

Azevedo, M. H., Soares, M. J., Coelho, I., Dourado, A., Valente, J., Macedo, A., ... & Pato, C. (1999). Using consensus OPCRIT diagnoses. An efficient procedure for best-estimate lifetime diagnoses. *The British Journal of Psychiatry*, *175*(2), 154-157.

Bailer, J., Bräuer, W., & Rey, E. R. (1996). Premorbid adjustment as predictor of outcome in schizophrenia: results of a prospective study. *Acta Psychiatrica Scandinavica*, *93*(5), 368-377.

Ballageer, T., Malla, A., Manchanda, R., Takhar, J., & Haricharan, R. (2005). Is adolescent-onset first-episode psychosis different from adult onset?. *Journal of the American Academy of Child & Adolescent Psychiatry*, *44*(8), 782-789.

Bardenstein, K. K., & McGlashan, T. H. (1990). Gender differences in affective, schizoaffective, and schizophrenic disorders: a review. *Schizophrenia Research*, *3*(3), 159-172.

Barnes, T. R., Hutton, S. B., Chapman, M. J., Mutsatsa, S., Puri, B. K., & Joyce, E. M. (2000). West London first-episode study of schizophrenia Clinical correlates of duration of untreated psychosis. *The British Journal of Psychiatry*, *177*(3), 207-211.

Basher, T. (1973). Psychiatric Services in Saudi Arabia. World Health Organization. Eastern Mediterranean Regional Office Report.

Bauer, S. M., Schanda, H., Karakula, H., Olajossy-Hilkesberger, L., Rudaleviciene, P., Okribelashvili, N., ... & Stompe, T. (2011). Culture and the prevalence of hallucinations in schizophrenia. *Comprehensive psychiatry*, *52*(3), 319-325.

Bazzoui, W., & Al-Issa, I. (1966). Psychiatry in Iraq. *The British Journal of Psychiatry*, *112*(489), 827-832.

Beratis, S., Gabriel, J., & Hoidas, S. (1997). Gender differences in the frequency of schizophrenic subtypes in unselected hospitalized patients. *Schizophrenia research*, *23*(3), 239-244.

Bleuler, E. (1950). Dementia praecox or the group of schizophrenias. (Trans. J. Zinkin), Zinkin J, editor. New York, NY: International Universities Press; 1950.

Boonstra, N., Klaassen, R., Sytema, S., Marshall, M., De Haan, L., Wunderink, L., & Wiersma, D. (2012). Duration of untreated psychosis and negative symptoms—a systematic review and meta-analysis of individual patient data. *Schizophrenia research*, *142*(1), 12-19.

Boydell, J., Bebbington, P., Bhavsar, V., Kravariti, E., van Os, J., Murray, R. M., & Dutta, R. (2013). Unemployment, ethnicity and psychosis. *Acta psychiatrica Scandinavica*, *127*(3), 202-209.

Boydell, J., Van Os, J., McKenzie, K., & Murray, R. M. (2004). The association of inequality with the incidence of schizophrenia. *Social Psychiatry And Psychiatric Epidemiology*, *39*(8), 597-599.

Boydell, J., Van Os, J., McKenzie, K., Allardyce, J., Goel, R., McCreadie, R. G., & Murray, R. M. (2001). Incidence of schizophrenia in ethnic minorities in London: ecological study into interactions with environment. *British Medical Journal*, *323*(7325), 1336.

Brittain, P. J., Lobo, S. E. M., Rucker, J., Amarasinghe, M., Anilkumar, A. P. P., Baggaley, M., ... & Schumann, G. (2013a). Harnessing Clinical Psychiatric Data with an Electronic Assessment Tool (OPCRIT+): The Utility of Symptom Dimensions. *PloS one*, *8*(3), e58790.

Brittain, P. J., Stahl, D., Rucker, J., Kawadler, J., & Schumann, G. (2013b). A review of the reliability and validity of OPCRIT in relation to its use for the routine clinical assessment of mental health patients. *International Journal Of Methods In Psychiatric Research*, *22*(2), 110-137.

Brohan, E., Slade, M., Clement, S., & Thornicroft, G. (2010). Experiences of mental illness stigma, prejudice and discrimination: a review of measures. *BMC Health Services Research*, *10*(1), 80.

Bromet, E., Harrow, M., & Kasl, S. (1974). Premorbid functioning and outcome in schizophrenics and nonschizophrenics. *Archives of General Psychiatry*, *30*(2), 203-207.

Buchanan , R and Carpenter, W (2005). Schizophrenia and other Psychotic Disorders . In Kaplan & Sadock's Comprehensive Textbook of Psychiatry (8th ed). Editors Benjamin Sadock and Vircinia Sadock . Vol 1 : Lippincott Williams & Wilkins. New York

Burns, J. K., Jhazbhay, K., & Emsley, R. A. (2011). Causal attributions, pathway to care and clinical features of first-episode psychosis: A South African perspective. *International Journal Of Social Psychiatry*, *57*(5), 538-545.

Cantor-Graae, E., & Selten, J. P. (2005). Schizophrenia and migration: a meta-analysis and review. *American Journal of Psychiatry*, *162*(1), 12-24.

Cardno, A. G., Holmans, P. A., Harvey, I., Williams, M. B., Owen, M. J., & McGuffin, P. (1997). Factor-derived subsyndromes of schizophrenia and familial morbid risks. *Schizophrenia Research*, *23*(3), 231-238.

Cardno, A. G., Jones, L. A., Murphy, K. C., Asherson, P., Scott, L. C., Williams, J., ... & McGuffin, P. (1996). Factor analysis of schizophrenic symptoms using the OPCRIT checklist. *Schizophrenia Research*, *22*(3), 233-239.

Cardno, A. G., Jones, L. A., Murphy, K. C., Sanders, R. D., Asherson, P., Owen, M. J., & McGuffin, P. (1999). Dimensions of psychosis in affected sibling pairs. *Schizophrenia Bulletin*, *25*(4), 841-850.

Cardno, A. G., Sham, P. C., Murray, R. M., & McGuffin, P. E. (2001). Twin study of symptom dimensions in psychoses. *The British Journal of Psychiatry*, *179*(1), 39-45.

Carpenter, W. T., Bartko, J. J., Carpenter, C. L., & Strauss, J. S. (1976). Another view of schizophrenia subtypes: a report from the International Pilot Study of Schizophrenia. *Archives of General Psychiatry*, *33*(4), 508-516.

Cascio, M. T., Cella, M., Preti, A., Meneghelli, A., & Cocchi, A. (2012). Gender and duration of untreated psychosis: a systematic review and meta-analysis. *Early Intervention In Psychiatry*, *6*(2), 115-127.

Castle, D. J., Abel, K., Takei, N., & Murray, R. M. (1995). Gender differences in schizophrenia: hormonal effect or subtypes? *Schizophrenia Bulletin*, *21*(1), 1.

Castle, D., Sham, P., & Murray, R. (1998). Differences in distribution of ages of onset in males and females with schizophrenia. *Schizophrenia research*, *33*(3), 179-183.

Central Department of Statistics & Information CDSI (2010). Ministry of Economy and Planning.

Central Department of Statistics & Information CDSI (2013). Ministry of Economy and Planning.

Chaleby, K., & Tuma, T. A. (1987). Cousin marriages and schizophrenia in Saudi Arabia. *The British Journal of Psychiatry*, *150*(4), 547-549.

Chen, E.Y-H., Dunn, E.L-W., Miao, M.Y-K., Yeung, W-S., Wong, C-K., Chan, W-F., Chen, R.Y-L., Chung, K-F., & Tang, W-N. (2005). The impact of family experience on the duration of untreated psychosis (DUP) in Hong Kong. *Social Psychiatry and Psychiatric Epidemiology*, *40*, 350-356.

Chilae, H., Banda, R., Muyawa, J ., Kaminga,A . (2014). Duration of Untreated Psychosis and Associated Factors in First Episode Psychosis in Mzuzu in Northern Malawi .*African Journal of Psychiatry* :17:503-507.

Chiliza, B., Asmal, L., & Emsley, R. (2012). Early intervention in schizophrenia in developing countries: Focus on duration of untreated psychosis and remission as a treatment goal. *International Review of Psychiatry*, *24*(5), 483-488.

Chiang, J. C. S., Chow, A. S., Chan, R. C., Law, C. W., & Chen, E. Y. (2005). Pathway to care for patients with first-episode psychosis in Hong Kong. *Hong Kong Journal of Psychiatry*, *15*(1), 18.

Chong, S. A., Lum, A., Chan, Y. H., & McGorry, P. (2005). Determinants of duration of untreated psychosis and the pathway to care in Singapore. *International Journal of Social Psychiatry*, *51*(1), 55-62.

Chowdhury, A. K. (1966). Admissions to an East Pakistan mental hospital. *The British Journal of Psychiatry*, *112*(482), 65-68.

Clark, R. E. (1948). The relationship of schizophrenia to occupational income and occupational prestige. *American Sociological Review*, 325-330.

Clark, R. E. (1949). Psychoses, income, and occupational prestige. *American journal of sociology*, 433-440.

Cochrane, R., & Bal, S. S. (1988). Ethnic density is unrelated to incidence of schizophrenia. *The British Journal of Psychiatry*, *153*(3), 363-366.

Cohen, A., Patel, V., Thara, R., & Gureje, O. (2008). Questioning an axiom: better prognosis for schizophrenia in the developing world?. *Schizophrenia Bulletin*, *34*(2), 229-244.

Cooper, J. E., Goodhead, D., Craig, T., Harris, M., Howat, J., & Korer, J. (1987). The incidence of schizophrenia in Nottingham. *The British Journal of Psychiatry*, *151*(5), 619-626.

Cooper, J., & Sartorius, N. (1977). Cultural and temporal variations in schizophrenia: a speculation on the importance of industrialization. *The British Journal of Psychiatry*, *130*(1), 50-55.

Craddock, M., Asherson, P., Owen, M. J., Williams, J., McGuffin, P., & Farmer, A. E. (1996). Concurrent validity of the OPCRIT diagnostic system. Comparison of OPCRIT diagnoses with consensus best-estimate lifetime diagnoses. *The British Journal of Psychiatry*, *169*(1), 58-63.

Craig, T. J., Bromet, E. J., Fenning, S., et al (2000) Is there an association between duration of untreated psychosis and 24-month clinical outcome in a first-admission series? American Journal of Psychiatry, 157, 60– 66.

Crisp, A. H., Gelder, M. G., Rix, S., Meltzer, H. I., & Rowlands, O. J. (2000). Stigmatisation of people with mental illnesses. *The British Journal of Psychiatry*, *177*(1), 4-7.

Croudace, T. J., Kayne, R., Jones, P. B., & Harrison, G. L. (2000). Non-linear relationship between an index of social deprivation, psychiatric admission prevalence and the incidence of psychosis. *Psychological medicine*, *30*(01), 177-185.

Crow, T. J. (1980). Molecular pathology of schizophrenia: more than one disease process?. *BMJ*, *280*(6207), 66-68.

Crow, T. J. (1985). The two-syndrome concept: origins and current status. *Schizophrenia bulletin*, *11*(3), 471.

Crow, T. J., MacMillan, J. F., Johnson, A. L., & Johnstone, E. C. (1986). A randomised controlled trial of prophylactic neuroleptic treatment. *The British Journal of Psychiatry*, *148*(2), 120-127.

Cutting, J. (1990). *The right cerebral hemisphere and psychiatric disorders*. Oxford University Press.

Dauncey, K. A. R. E. N., Giggs, J., Baker, K. A. R. E. N., & Harrison, G. (1993). Schizophrenia in Nottingham: lifelong residential mobility of a cohort. *The British Journal of Psychiatry*, *163*(5), 613-619.

De Haan, L., Welborn, K., Krikke, M., & Linszen, D. H. (2004). Opinions of mothers on the first psychotic episode and the start of treatment of their child. *European Psychiatry*, *19*(4), 226-229.

Dekker, J., Peen, J., Koelen, J., Smit, F., & Schoevers, R. (2008). Psychiatric disorders and urbanization in Germany. *Bmc Public Health*, *8*(1), 17.

Demjaha, A., Morgan, K., Morgan, C., Landau, S., Dean, K., & Reichenberg, A. et al. (2009). Combining dimensional and categorical representation of psychosis: the way forward for DSM-V and ICD-11?. *Psychological Medicine*, *39*(12), 1943--1955.

Dendle, P. (2005). Schizophrenia in the early middle ages: some negative evidence. *Australian and New Zealand Journal of Psychiatry*, *39*(6), 522.

Dikeos, D. G., Wickham, H., McDONALD, C. O. L. M., Walshe, M., Sigmundsson, T., Bramon, E., ... & Sham, P. C. (2006). Distribution of symptom dimensions across Kraepelinian divisions. *The British Journal of Psychiatry*, *189*(4), 346-353

Dohrenwend, B. P., & Dohrenwend, B. S. (1976). Sex differences and psychiatric disorders. *American journal of Sociology*, 1447-1454.

Dohrenwend, B. P., Levav, I., Shrout, P. E., Schwartz, S., Naveh, G., Link, B. G., ... & Stueve, A. (1992). Socioeconomic status and psychiatric disorders: the causation-selection issue. *Science(Washington)*, *255*(5047), 946-952.

Dols, M. W. (1987). The origins of the Islamic hospital: myth and reality. *Bulletin of the History of Medicine*, *61*(3), 367-390.

Dols, M. W. (1992). *Majnun: The madman in medieval Islamic society* (p. 294). D. E. Immisch (Ed.). Oxford: Clarendon Press.

Dominguez, M. D. G., Fisher, H. L., Major, B., Chisholm, B., Rahaman, N., Joyce, J., ... & Hodes, M. (2013). Duration of untreated psychosis in adolescents: Ethnic differences and clinical profiles. *Schizophrenia Research*, *150*(2), 526-532.

Drake, R. J., Haley, C. J., Akhtar, S., & Lewis, S. W. (2000). Causes and consequences of duration of untreated psychosis in schizophrenia. *The British Journal of Psychiatry*, *177*(6), 511-515.

Drukker, M., Krabbendam, L., Driessen, G., & van Os, J. (2006). Social disadvantage and schizophrenia. *Social psychiatry and psychiatric epidemiology*, *41*(8), 595-604.

Dunham, H. W. (1966). Epidemiology of psychiatric disorders as a contribution to medical ecology. *Archives Of General Psychiatry*, *14*(1), 1-9.

Eaton, W. W. (1999). Evidence for universality and uniformity of schizophrenia around the world: assessment and implications. In *Search for the Causes of Schizophrenia* (pp. 21-33). Steinkopff.

El-Adl, M., & Balhaj, T. (2008). Stigma of mental illness (SMI): views of the public in an Arabic culture. *Arab Journal of Psychiatry*, *19*, 57-65.

El-Islam, M. F. (2008). Arab culture and mental health care. *Transcultural psychiatry*, *45*(4), 671-682.

El-Islam, M., Abu-Dagga, S., Malsi, T., & Moussa, M.(1986). Intergenerational conflict and psychiatric syndromes. *The British Journal of Psychiatry,149:300-306.*

Evans, K., McGrath, J., & Milns, R. (2003). Searching for schizophrenia in ancient Greek and Roman literature: a systematic review. *Acta Psychiatrica Scandinavica*, *107*(5), 323-330.

Faris, R. E. L., & Dunham, H. W. (1939). Mental disorders in urban areas: an ecological study of schizophrenia and other psychoses. Chicago: University of Chicago Press

Farmer, A. E., Jones, I., Williams, J., & McGuffin, P. (1993). Defining schizophrenia: Operational criteria. *Journal of Mental Health*, *2*(3), 209-222.

Fawzi, M. M., El-Amin, H. M., & Fawzi, M. H. (2011). Duration of untreated psychosis in two Arab samples from Egypt and Saudi Arabia: Clinical and sociocultural correlates. *Middle East Current Psychiatry*, *18*(4), 217-225.

Fearon, P., Kirkbride, J. B., Morgan, C., Dazzan, P., Morgan, K., Lloyd, T., ... & Murray, R. M. (2006). Incidence of schizophrenia and other psychoses in ethnic minority groups: results from the MRC AESOP Study. *Psychological Medicine*, *36*(11), 1541-1550.

Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Winokur, G., & Munoz, R. (1972). Diagnostic criteria for use in psychiatric research. *Archives of general psychiatry*, *26*(1), 57-63.

Flor-Henry, P. (1990). Influence of gender in schizophrenia as related to other psychopathological syndromes. *Schizophrenia Bulletin*, *16*(2), 211-227.

Fortney, J., Rushton, G., Wood, S., Zhang, L., Xu, S., Dong, F., & Rost, K. (2007). Community-level risk factors for depression hospitalizations. *Administration and Policy in Mental Health and Mental Health Services Research*, *34*(4), 343-352.

Fortney, J., Xu, S., & Dong, F. (2009). Community-level correlates of hospitalizations for persons with schizophrenia. *Psychiatric Services*, *60*(6), 772-778.

Fowler, R. C., McCabe, M. S., Cadoret, R. J., & Winokur, G. (1972). The validity of good prognosis schizophrenia. *Archives of General Psychiatry*, *26*(2), 182-185.

Gagne, C., Hopper, K., Harrison, G., Janca, A., & Satorius, N. (2007). Recovery from schizophrenia: An international perspective. *Psychiatric Rehabilitation Journal*, *31*(1), 85-86.

Gater, R., Amaddeo, F., Tansella, M., Jackson, G., & Goldberg, D. (1995). A comparison of community-based care for schizophrenia in south Verona and south Manchester. *The British Journal of Psychiatry*, *166*(3), 344-352.

Geddes, J. R., & Kendell, R. E. (1995). Schizophrenic subjects with no history of admission to hospital. *Psychological Medicine*, *25*(04), 859-868.

Ghubash, R., Hamdi, E., & Bebbington, P. (1992). The Dubai community psychiatric survey: I. Prevalence and socio-demographic correlates. *Social Psychiatry And Psychiatric Epidemiology*, *27*(2), 53-61.

Goldacre, M., Shiwach, R., & Yeates, D. (1994). Estimating incidence and prevalence of treated psychiatric disorders from routine statistics: the example of schizophrenia in Oxfordshire. *Journal Of Epidemiology And Community Health*, *48*(3), 318-322.

Goldberg, T. E., David, A., & Gold, J. M. (1995). Neurocognitive deficits in schizophrenia. *Schizophrenia, Second Edition*, 168-184.

Goldner, E., Hsu, L., Waraich, P., Somers, J. (2002). Prevalence and incidence studies of schizophrenic disorders: asystematic review of the literature. *Canadian Journal of Psychiatry*, 47:833–843.

Goldstein, J. M., Tsuang, M. T., & Faraone, S. V. (1989). Gender and schizophrenia: implications for understanding the heterogeneity of the illness. *Psychiatry Research*, *28*(3), 243-253.

Gove, W. R. (1972). The relationship between sex roles, marital status, and mental illness. *Social forces*, *51*(1), 34-44.

Grube, B. S., Bilder, R. M., & Goldman, R. S. (1998). Meta-analysis of symptom factors in schizophrenia. *Schizophrenia research*, *31*(2), 113-120.

Guggenheim, F. G., & Babigian, H. M. (1974). Catatonic schizophrenia: epidemiology and clinical course: a 7-year register study of 798 cases. *The Journal of nervous and mental disease*, *158*(4), 291-305.

Gureje, O., Acha, R. A., & Odejide, O. A. (1995). Pathways to psychiatric care in Ibadan, Nigeria. *Tropical and geographical medicine*, *47*(3), 125-129.

Gureje, O., & Bamidele, R. (1999). Thirteen-year social outcome among Nigerian outpatients with schizophrenia. *Social Psychiatry And Psychiatric Epidemiology*, *34*(3), 147-151.

Gureje, O., Lasebikan, V. O., Ephraim-Oluwanuga, O., Olley, B. O., & Kola, L. (2005). Community study of knowledge of and attitude to mental illness in Nigeria. *The British Journal of Psychiatry*, *186*(5), 436-441.

Häfner, H., & Reimann, H. (1970). Spatial distribution of mental disorders in Mannheim, 1965. *Psychiatric epidemiology*, *1*.

Häfner, H., Maurer, K., Löffler, W., & Fätkenheuer, B. (1994). The epidemiology of early schizophrenia influence of age and gender on onset and early course. *The British journal of psychiatry*.

Häfner,H., Maurer, K., Löffler, W., Riecher-Rossler,A. (1993).The influence of age and sex on the onset and early course of schizophrenia. British Journal of Psychiatry 162, 80-86

Hales, R. E., Yudofsky, S. C., & Gabbard, G. O. (Eds.). (2008). *The American psychiatric publishing textbook of psychiatry*. American Psychiatric Pub.

Halpern, D. (1993). Minorities and mental health. *Social science & medicine*, *36*(5), 597-607.

Hannawi, S., & Salmi, I. A. (2013). Health workforce in the United Arab Emirates: analytic point of view. *The International journal of health planning and management*.

Hare, E. H. (1956a). Family setting and the urban distribution of schizophrenia. *The British Journal of Psychiatry*, *102*(429), 753-760.

Hare, E. H. (1956b). Mental illness and social conditions in Bristol. *The British Journal of Psychiatry*, *102*(427), 349-357.

Hare, E. H. (1988). Schizophrenia as a recent disease. *The British Journal of Psychiatry*, *153*(4), 521-531

Harrison, G., Hopper, K., Craig, T., Laska, E., Siegel, C., Wanderling, J., ... & Wiersma, D. (2001). Recovery from psychotic illness: a 15-and 25-year international follow-up study. *The British Journal of Psychiatry*, *178*(6), 506-517.

Harrison, G., Owens, D., Holton, A., Neilson, D., & Boot, D. (1988). A prospective study of severe mental disorder in Afro-Caribbean patients. *Psychological Medicine*, *18*(03), 643-657.

Harvey, P. D., Helldin, L., Bowie, C. R., Heaton, R. K., Olsson, A. K., Hjärthag, F., ... & Patterson, T. L. (2009). Performance-based measurement of functional disability in schizophrenia: a cross-national study in the United States and Sweden. *American Journal of Psychiatry*, *166*(7), 821-827.

Henderson, C., Thornicroft, G., & Glover, G. (1998). Inequalities in mental health. *The British Journal of Psychiatry*, *173*(2), 105-109.

Herz, M. I., & Marder, S. R. (2002). Schizophrenia: comprehensive treatment and management.

Hinsie, L. E., & Campbell, R. J. (1970). Psychiatric dictionary. Fourth Edition, Oxford University Press. New York

Hirsch, S & Weinberger, D (1995) Schizophrenia . Blacwell Science.England.

Hitch, P. J., & Rack, P. H. (1980). Mental illness among Polish and Russian refugees in Bradford. *The British Journal of Psychiatry*, *137*(3), 206-211.

Ho, B., Andreasen, N. C., Flaum, M., et al (2000) Untreated initial psychosis: its relation to quality of life and symptom remission in first-episode schizophrenia. *American Journal Of Psychiatry*, 157, 808 -815.

Ho, B. C., Alicata, D., Ward, J., Moser, D. J., O'Leary, D. S., Arndt, S., & Andreasen, N. C. (2003). Untreated initial psychosis: relation to cognitive deficits and brain morphology in first-episode schizophrenia. *American Journal of Psychiatry*.

Hollingshead, A. B., & Redlich, F. C. (1954). Schizophrenia and social structure. *American Journal of Psychiatry*, *110*(9), 695-701.

Hollingshead, A. B., & Redlich, F. C. (2007). Social class and mental illness: a community study. *American journal of public health*, *97*(10), 1756-1757.

Hollis, C. (2000) Adolescent schizophrenia. Advances in Psychiatric Treatment, 6, 83–92.

Hopper, K., Harrison, G., Janca, A., & Sartorius, N. (2007). Recovery from schizophrenia: An international perspective. A report from the WHO Collaborative Project, the International Study of Schizophrenia. *Annals of Clinical Psychiatry*, *19*(3), 209.

Howells, J .(1991) The concept of schizophrenia: historical perspectives. Washington, DC: American Psychiatric Press

Hussein, F. (1989). A study of the role of unorthodox treatments of psychiatric illnesses. *Arab Journal of Psychiatry*, 2:170-184

Hutchinson, G., Takei, N., Sham, P., Harvey, I., & Murray, R. M. (1999). Factor analysis of symptoms in schizophrenia: differences between White and Caribbean patients in Camberwell. *Psychological medicine*, *29*(03), 607-612.

Iacono, W. G., & Beiser, M. (1992). Are males more likely than females to develop schizophrenia?. *The American journal of psychiatry*.

Isohanni, M., Mäkikyrö, T., Moring, J., Räsanen, P., Hakko, H., Partanen, U., ... & Jones, P. (1997). A comparison of clinical and research DSM-III-R diagnoses of schizophrenia in a Finnish national birth cohort. *Social psychiatry and psychiatric epidemiology*, *32*(5), 303-308.

Jablensky, A. (1999) Psychiatric epidemiology and the global public health agenda. *International Journal of Mental Health*, 28, 6 -14.

Jablensky, A., Sartorius, N., Ernberg, G., Anker, M., Korten, A., Cooper, J. E., ... & Bertelsen, A. (1992). Schizophrenia: manifestations, incidence and course in different cultures A World Health Organization Ten-Country Study. *Psychological medicine. Monograph supplement*, *20*, 1-97.

Jackson, H. J., & McGorry, P. D. (2009). *The recognition and management of early psychosis: a preventive approach*. Cambridge University Press.

Jaco, E. G. (1954). The social isolation hypothesis and schizophrenia. *American Sociological Review*, 567-577.

Jeste, D. V., Del Carmen, R., Lohr, J. B., & Wyatt, R. J. (1985). Did schizophrenia exist before the eighteenth century?. *Comprehensive psychiatry*, *26*(6), 493-503.

Jia, H., Moriarty, D. G., & Kanarek, N. (2009). County-level social environment determinants of health-related quality of life among US adults: a multilevel analysis. *Journal of community health*, *34*(5), 430-439.

Johnstone, E. C., Frith, C. D., Lang, F. H., & Owens, D. G. (1995). Determinants of the extremes of outcome in schizophrenia. *The British Journal of Psychiatry*, *167*(5), 604-609.

Jones, P. B., Bebbington, P., Foerster, A., Lewis, S. W., Murray, R. M., Russell, A., ... & Wilkins, S. (1993). Premorbid social underachievement in schizophrenia. Results from the Camberwell Collaborative Psychosis Study. *The British Journal of Psychiatry*, *162*(1), 65-71.

Jorm, A. F., Korten, A. E., Jacomb, P. A., Christensen, H., & Henderson, S. (1999). Attitudes towards people with a mental disorder: a survey of the Australian public and health professionals. *Australian and New Zealand Journal of Psychiatry*, *33*(1), 77-83.

Kadri, N., Manoudi, F., Berrada, S., & Moussaoui, D. (2004). Stigma impact on Moroccan families of patients with schizophrenia. *Canadian Journal of Psychiatry*, *49*, 625-629.

Kavanagh, D. J. (1992). *Schizophrenia: An overview and practical handbook*. Chapman & Hall.

Kay, S. R., Flszbein, A., & Opfer, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia bulletin*, *13*(2), 261.

Kay, S. R., & Sevy, S. (1990). Pyramidical model of schizophrenia. *Schizophrenia Bulletin*, *16*(3), 537.

Keefe, R & Harvey, P (1994) Understanding schizophrenia: a guide to the new research on causes and treatment. Simon & Schuster Inc. New York

Kelly, B. D., O'Callaghan, E., Waddington, J. L., Feeney, L., Browne, S., Scully, P. J., ... & Larkin, C. (2010). Schizophrenia and the city: A review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophrenia research*, *116*(1), 75-89.

Kendell, R. E., Malcolm, D. E., & Adams, W. (1993). The problem of detecting changes in the incidence of schizophrenia. *The British Journal of Psychiatry*, *162*(2), 212-218.

Kendler, K. S., & Diehl, S. R. (1993). The genetics of schizophrenia. *Schizophrenia Bulletin*, *19*(2), 261-285.

Kendler, K. S., & Tsuang, M. T. (1988). Outcome and familial psychopathology in schizophrenia. *Archives Of General Psychiatry*, *45*(4), 338-346.

Kent, G., & Wahass, S. (1996). The content and characteristics of auditory hallucinations in Saudi Arabia and the UK: a cross-cultural comparison. *Acta Psychiatrica Scandinavica*, *94*(6), 433-437.

Keshavan, M. S., & Schooler, N. R. (1992). First-episode studies in schizophrenia: criteria and characterization. *Schizophrenia Bulletin*, *18*(3), 491-513.

Keshavan, M. S., Stanley, J. A., Montrose, D. M., Minshew, N. J., & Pettegrew, J. W. (2003). Prefrontal membrane phospholipid metabolism of child and adolescent offspring at risk for schizophrenia or schizoaffective disorder: an in vivo 31P MRS study. *Molecular Psychiatry*, *8*(3), 316-323.

King, M., Coker, E., Leavey, G., Hoare, A., & Johnson-Sabine, E. (1994). Incidence of psychotic illness in London: comparison of ethnic groups. *British Medical Journal*, *309*(6962), 1115-1119.

Kirkbride, J. B., Barker, D., Cowden, F., Stamps, R., Yang, M., Jones, P. B., & Coid, J. W. (2008). Psychoses, ethnicity and socio-economic status. *The British Journal of*

Psychiatry, *193*(1), 18-24.

Kirkbride, J. B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., ... & Jones, P. B. (2012). Incidence of schizophrenia and other psychoses in England, 1950–2009: a systematic review and meta-analyses. *PloS one*, *7*(3), e31660.

Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., ... & Jones, P. B. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AESOP study. *Archives of general psychiatry*, *63*(3), 250-258.

Klee, G. D., Spiro, E., Bahn, A. K., & Gorwitz, K. (1967). An ecological analysis of diagnosed mental illness in Baltimore. *Psychiatric research reports*, *22*, 107.

Koenig, H. G. (2009). *Faith and mental health: Religious resources for healing*. Templeton Foundation Press.

Kopelowicz, A., Ventura, J., Liberman, R. P., & Mintz, J. (2008). Consistency of Brief Psychiatric Rating Scale factor structure across a broad spectrum of schizophrenia patients. *Psychopathology*, *41*(2), 77-84.

Køster, A., Lajer, M., Lindhardt, A., & Rosenbaum, B. (2008). Gender differences in first episode psychosis. *Social psychiatry and psychiatric epidemiology*, *43*(12), 940-946.

Krabbendam, L., & Van Os, J. (2005). Schizophrenia and urbanicity: a major environmental influence—conditional on genetic risk. *Schizophrenia bulletin*, *31*(4), 795-799.

Kraepelin, E. (1913) Psychiatric (8th edn). Translated by R. M. Barclay (1919) from vols 3, part 2 as Dementia Praecox and Paraphrenia. Edinburgh: Livingstone.

Kremen, W. S., Seidman, L. J., Pepple, J. R., Lyons, M. J., Tsuang, M. T., & Faraone, S. V. (1994). Neuropsychological risk indicators for schizophrenia. *Schizophrenia Bulletin*, *20*(1), 103-119.

Kroeber, A. L., & Kluckhohn, C. (1952). Culture: A critical review of concepts and definitions. *Papers. Peabody Museum of Archaeology & Ethnology, Harvard University*.

Kurihara, T., Kato, M., Reverger, R., & Tirta, I. G. R. (2005). Eleven-year clinical outcome of schizophrenia in Bali. *Acta Psychiatrica Scandinavica*, *112*(6), 456-462.

Kyziridis, T. C. (2005). Notes on the history of schizophrenia. *German Journal of Psychiatry*, *8*(3), 8-42.

Laird, J. T. (1973). Mental health and population density. *The Journal of psychology*, *85*(2), 171-177.

Larsen, T. K., McGlashan, T. H., Johannessen, J. O., & Vibe-Hansen, L. (1996). First-episode schizophrenia: II. Premorbid patterns by gender. *Schizophrenia Bulletin*, *22*(2), 257.

Lastra, I., Nu, M. C., Castanedo, S. H., & Dunn, G. (1996). Patterns of positive and negative symptoms in first episode schizophrenia. *The British Journal of Psychiatry*, *168*(6), 693-701.

Leung, M. D., & Psych, C. M. (2000). Sex differences in schizophrenia, a review of the literature. *Acta Psychiatrica Scandinavica*, *101*(401), 3-38.

Lewine, R. R. (1981). Sex differences in schizophrenia: timing or subtypes?. *Psychological Bulletin*, *90*(3), 432.

Lewine, R., Burbach, D., & Meltzer, H. Y. (1984). Effect of diagnostic criteria on the ratio of male to female schizophrenic patients," *American Journal of Psychiatry*,141(1),84–87.

Lewine, R., Haden, C., Caudle, J., & Shurett, R. (1997). Sex-onset effects on neuropsychological function in schizophrenia. *Schizophrenia bulletin*, *23*(1), 51-61.

Lewis, G., David, A., Andréassson, S., & Allebeck, P. (1992). Schizophrenia and city life. *The Lancet*, *340*(8812), 137-140.

Lewis, S. W., & Buchanan, R. W. (2005). Fast facts: schizophrenia, 2nd edn. *Australian and New Zealand Journal of Psychiatry*, *39*(7).

Liddle, P. F. (1987). The symptoms of chronic schizophrenia. A re-examination of the positive-negative dichotomy. *The British Journal of Psychiatry*, *151*(2), 145-151.

Lindenmayer, J. P., Bernstein-Hyman, R., & Grochowski, S. (1994). Five-Factor Model of Schizophrenia Initial Validation. *The Journal of nervous and mental disease*, *182*(11), 631-638.

Lindström, E., & Knorring, L. V. (1993). Principal component analysis of the Swedish version of the Positive and Negative Syndrome Scale for schizophrenia. *Nordic Journal of Psychiatry*, *47*(4), 257-263.

Loebel, A. D., Lieberman, J. A., Alvir, J. M., Mayerhoff, D. I., Geisler, S. H., & Szymanski, S. R. (1992). Duration of psychosis and outcome in first-episode schizophrenia. *The American journal of psychiatry*, *149*(9), 1183.

Lofors, J., & Sundquist, K. (2007). Low-linking social capital as a predictor of mental disorders: a cohort study of 4.5 million Swedes. *Social science & medicine*, *64*(1), 21-34.

Loranger, A. W. (1984). Sex difference in age at onset of schizophrenia. *Archives of General Psychiatry*, *41*(2), 157-161.

Losert, C., Schmauß, M., Becker, T., & Kilian, R. (2012). Area characteristics and admission rates of people with schizophrenia and affective disorders in a

German rural catchment area. *Epidemiology and psychiatric sciences*, *21*(4), 371-379.

MacCabe, J. H., Aldouri, E., Fahy, T. A., Sham, P. C., & Murray, R. M. (2002). Do schizophrenic patients who managed to get to university have a non-developmental form of illness?. *Psychological medicine*, *32*(03), 535-544.

MacMahon, B., & Pugh, T. F. (1970). Epidemiology: principles and methods. Littke , Brown and company, Boston .

Malla, A. K., Norman, R. M., Manchanda, R., Ahmed, M. R., Scholten, D., Harricharan, R., ... & Takhar, J. (2002). One year outcome in first episode psychosis: influence of DUP and other predictors. *Schizophrenia Research*, *54*(3), 231-242.

Malzberg, B. (1936). Marital status in relation to the prevalence of mental illness. *Psychiatric Quarlerly,*(10,)245-261

Mansour, A. (2008). High schoolers knowledge and attitudes about schizophrenia in Saudi Arabia. *Bull Alexandria Faculty of Medicine*, *44*(3).

Marcelis, M., Navarro-Mateu, F., Murray, R., Selten, J. P., & van Os, J. (1998). Urbanization and psychosis: a study of 1942–1978 birth cohorts in The Netherlands. *Psychological medicine*, *28*(04), 871-879.

March, D., Hatch, S. L., Morgan, C., Kirkbride, J. B., Bresnahan, M., Fearon, P., & Susser, E. (2008). Psychosis and place. *Epidemiologic Reviews*, *30*(1), 84-100.

Marwaha, S., Johnson, S., Bebbington, P. E., Angermeyer, M. C., Brugha, T. S., Azorin, J. M., ... & Toumi, M. (2009). Predictors of employment status change over 2 years in people with schizophrenia living in Europe. *Epidemiologia e psichiatria sociale*, *18*(04), 344-351.

Mass, R., Schoemig, T., Hitschfeld, K., Wall, E., & Haasen, C. (2000). Psychopathological syndromes of schizophrenia: evaluation of the dimensional structure of the positive and negative syndrome scale. *Schizophrenia Bulletin*, *26*(1), 167-177.

Maurer, K., & Riecher-R, A. (1993). The influence of age and sex on the onset and early course of schizophrenia. *The British journal of psychiatry*, *162*(1), 80-86

Mbewe, E., Haworth, A., Welham, J., Mubanga, D., Chazulwa, R., Zulu, M. M., ... & McGrath, J. (2006). Clinical and demographic features of treated first-episode psychotic disorders: a Zambian study. *Schizophrenia research*, *86*(1), 202-207.

McGlashan, T. H. (1999). Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course?. *Biological Psychiatry*, *46*(7), 899-907.

McGorry, P. D. (1998). "A stitch in time"… the scope for preventive strategies in early psychosis. *European Archives Of Psychiatry And Clinical Neuroscience*, *248*(1), 22-31.

McGrath, J. A., Nestadt, G., Liang, K. Y., Lasseter, V. K., Wolyniec, P. S., Fallin, M. D., ... & Pulver, A. E. (2004). Five latent factors underlying schizophrenia: analysis and relationship to illnesses in relatives. *Schizophrenia bulletin*, *30*(4), 855.

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiologic reviews*, *30*(1), 67-76.

McGrath, J., Saha, S., Welham, J., El Saadi, O., MacCauley, C., & Chant, D. (2004). A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Medicine*, *2*(1), 13.

McGuffin, P., Asherson, P., Owen, M., & Farmer, A. (1994). The strength of the genetic effect. Is there room for an environmental influence in the aetiology of schizophrenia?. *The British Journal Of Psychiatry*, *164*(5), 593-599.

McGuffin, P., Farmer, A., & Harvey, I. (1991). A polydiagnostic application of operational criteria in studies of psychotic illness: development and reliability of the OPCRIT system. *Archives Of General Psychiatry*, *48*(8), 764.

McGuffin, P., & Murray, R. (Eds.). (2013). *The new genetics of mental illness*. Butterworth-Heinemann.

Mclntosh, A. M., Forrester, A., Lawrie, S. M., Byrne, M., Harper, A., Kestelman, J. N., ... & Owens, D. G. C. (2001). A factor model of the functional psychoses and the relationship of factors to clinical variables and brain morphology. *Psychological medicine*, *31*(1), 159-171.

McKenna, P. J. (2007). *Schizophrenia and related syndromes*. Routledge.UK

Menezes, P. R., Rodrigues, L. C., & Mann, A. H. (1997). Predictors of clinical and social outcomes after hospitalization in schizophrenia. *European Archives Of Psychiatry And Clinical Neuroscience*, *247*(3), 137-145.

Minas, H., Klimidis, S., & Tuncer, C. (2007). Illness causal beliefs in Turkish immigrants. *BMC psychiatry*, *7*(1), 34.

Ministry of Health (2009). Health statistical year book. Riyadh, Ministry of Health.

Minzenberg, M.J., Yoon, J.H& Carter, C.S. (2008). Schizophrenia. In Hales, R. E *The American psychiatric publishing textbook of psychiatry*. (p273-310) .American Psychiatric Pub.

Mishara, A. L., & Corlett, P. (2009). Are delusions biologically adaptive? Salvaging the doxastic shear pin. *Behavioral and Brain Sciences*, *32*(06), 530-531.

Moilanen, K., Veijola, J., Läksy, K., Mäkikyrö, T., Miettunen, J., Kantojärvi, L., ... & Isohanni, M. (2003). Reasons for the diagnostic discordance between clinicians and researchers in schizophrenia in the Northern Finland 1966 Birth Cohort. *Social psychiatry and psychiatric epidemiology*, *38*(6), 305-310.

Morgan, C., Abdul-Al, R., Lappin, J. M., Jones, P., Fearon, P., Leese, M., ... & Murray, R. (2006). Clinical and social determinants of duration of untreated psychosis in the AESOP first-episode psychosis study. *The British Journal of Psychiatry*, *189*(5), 446-452.

Morgan, C., Dazzan, P., Morgan, K., Jones, P., Harrison, G., Leff, J., ... & Fearon, P. (2006). First episode psychosis and ethnicity: initial findings from the AESOP study. *World Psychiatry*, *5*(1), 40.

Morgan, G ., Fisher, H (2007)Environment and Schizophrenia: Environmental Factors in Schizophrenia: Childhood Trauma—A Critical Review Schizophr Bull ,33 (1): 3-10.

Morsy, S. A. (1993). *Gender, sickness, and healing in rural Egypt: Ethnography in historical context*. Boulder, CO, US: Westview Press.

Mortensen, P. B., Pedersen, C. B., Westergaard, T., Wohlfahrt, J., Ewald, H., Mors, O., ... & Melbye, M. (1999). Effects of family history and place and season of birth on the risk of schizophrenia. *New England Journal of Medicine*, *340*(8), 603-608.

Mortensen, P. B., Pedersen, C. B., Westergaard, T., Wohlfahrt, J., Ewald, H., Mors, O., ... & Melbye, M. (1999). Effects of family history and place and season of birth on the risk of schizophrenia. *New England Journal of Medicine*, *340*(8), 603-608.

Moscarelly, M., Rupp, A., & Sartorius, N. (1996). Handbook of Mental Health Economic and Health Policy, vol 1: Schizophrenia .New York : John Wiley& Sons.

Mueser, K. T., Curran, P. J., & McHugo, G. J. (1997). Factor structure of the Brief Psychiatric Rating Scale in schizophrenia. *Psychological Assessment*, *9*(3), 196.

Murphy, B. M., Burke, J. G., Bray, J. C., Walsh, D., & Kendler, K. S. (1994). An analysis of the clinical features of familial schizophrenia. *Acta Psychiatrica Scandinavica*, *89*(6), 421-427.

Murray, R. M., Jones, P. B., Susser, E., Van Os, J., & Cannon, M. (Eds.). (2002). *The epidemiology of schizophrenia*. Cambridge University Press.

Murray, V., McKee, I., Miller, P. M., Young, D., Muir, W. J., Pelosi, A. J., & Blackwood, D. H. R. (2005). Dimensions and classes of psychosis in a population cohort: a four-class, four-dimension model of schizophrenia and affective psychoses. *Psychological medicine*, *35*(04), 499-510.

Myers, N. (2011) Update:Schizophrenia Across cultures . Current Psychiatry Reports

Naqvi, H. A., Hussain, S., Zaman, M., & Islam, M. (2009). Pathways to care: Duration of untreated psychosis from Karachi, Pakistan. *PloS one*, *4*(10), e7409.

Nimgaonkar, V. L., Wessely, S., Tune, L. E., & Murray, R. M. (1988). Response to drugs in schizophrenia: the influence of family history, obstetric complications and ventricular enlargement. *Psychological Medicine*, *18*(03), 583-592.

Norman, R. M., TownsenD, L., & Malla, A. K. (2001). Duration of untreated psychosis and cognitive functioning in first-episode patients. *The British Journal of Psychiatry*, *179*(4), 340-345.

North, C., & Yutzy, S. (2009). *Goodwin and Guze's Psychiatric Diagnosis*. Oxford University Press.

Ochoa, S., Usall, J., Cobo, J., Labad, X., & Kulkarni, J. (2012). Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review. *Schizophrenia Research And Treatment*, *2012*.

Ohaeri, J. U. (1993). Long-term outcome of treated schizophrenia in a Nigerian cohort: retrospective analysis of 7-year follow-ups. *The Journal Of Nervous And Mental Disease*, *181*(8), 514-516.

Okasha, A. (2003). Psychiatric research in an international perspective. The role of WPA. *Acta Psychiatrica Scandinavica*, *107*(2), 81-84.

Okasha, A. (2004). Focus on psychiatry in Egypt. *The British Journal of Psychiatry*, *185*(3), 266-272.

Okasha, A. (2005). Globalization and mental health: a WPA perspective. *World Psychiatry*, *4*(1), 1.

Okasha, A., Kamel, M., & Hassan, A. H. (1968). Preliminary psychiatric observations in Egypt. *The British Journal of Psychiatry*, *114*(513), 949-955.

Parr, H., Philo, C., & Burns, N. (2004). Social geographies of rural mental health: experiencing inclusions and exclusions. *Transactions of the Institute of British Geographers*, *29*(4), 401-419.

Paul, K. I., & Moser, K. (2009). Unemployment impairs mental health: Meta-analyses. *Journal Of Vocational Behavior*, *74*(3), 264-282.

Paykel, E. S., Abbott, R., Jenkins, R., Brugha, T. S., & Meltzer, H. (2000). Urban–rural mental health differences in Great Britain: findings from the National Morbidity Survey. *Psychological Medicine*, *30*(02), 269-280.

Pedersen, C. B., & Mortensen, P. B. (2001). Family history, place and season of birth as risk factors for schizophrenia in Denmark: a replication and reanalysis. *The British Journal of Psychiatry*, *179*(1), 46-52.

Pek, E., Mythily, S., & Chong, S. A. (2006). Clinical and social correlates of duration of untreated psychosis in first-episode psychosis patients. *Annals-Academy Of Medicine Singapore*, *35*(1), 24.

Peralta, V., & Cuesta, M. (1998). Factor structure and clinical validity of competing models of positive symptoms in schizophrenia. *Biological Psychiatry*, *44*(2), 107-114.

Peralta, V., & Cuesta, M. J. (2001). How many and which are the psychopathological dimensions in schizophrenia? Issues influencing their ascertainment. *Schizophrenia Research*, *49*(3), 269-285.

Perkins, D. O., Gu, H., Boteva, K., & Lieberman, J. A. (2005). Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *American Journal of Psychiatry*.

Picker, J. (2005). The role of genetic and environmental factors in the development of schizophrenia. *Psychiatr Times*, *22*(9), 29-32.

Pridmore, S., & Pasha, M. I. (2004). Religion and spirituality: Psychiatry and Islam. *Australasian Psychiatry*, *12*(4), 381-385.

Primavera, D., Bandecchi, C., Lepori, T., Sanna, L., Nicotra, E., & Carpiniello, B. (2012). Does duration of untreated psychosis predict very long term outcome of schizophrenic disorders? results of a retrospective study. *Annals Of General Psychiatry*, *11*(1), 1-6.

Prince, M., & Phelan, M. (1994). Invisible schizophrenia: A postal survey of the incidence and management of new cases of schizophrenia in primary care. *Journal of Mental Health*, *3*(1), 91-98.

Pull, C. B. (2002). Diagnosis of schizophrenia: a review. *Schizophrenia. WPA Series Evidence and Experience in Psychiatry*, *2*, 1-72.

Qureshi, N. A., Al-Habeeb, A. A., & Koenig, H. G. (2013). Mental health system in Saudi Arabia: an overview. *Neuropsychiatric Disease And Treatment*, *9*, 1121.

Rabkin, J. G. (1979). Ethnic density and psychiatric hospitalization: hazards of minority status. *The American journal of psychiatry*, *136*(12), 1562-1566.

Ran, M., Xiang, M., Huang, M., & Shan, Y. (2001). Natural course of schizophrenia: 2-year follow-up study in a rural Chinese community. *The British Journal of Psychiatry*, *178*(2), 154-158.

Rao, S. (1966). Culture and mental disorder: A study in an Indian mental hospital. *International Journal of Social Psychiatry*, *12*(2), 139-148.

Räsänen, S., Veijola, J., Hakko, H., Joukamaa, M., & Isohanni, M. (1999). Gender differences in incidence and age of onset of DSM-III-R schizophrenia: Preliminary results of the Northern Finland 1966 birth cohort study. *Schizophrenia Research*, *37(*2), 197-198.

Read, J., Os, J. V., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica*, *112*(5), 330-350.

Reay, R., Mitford, E., McCabe, K., Paxton, R., & Turkington, D. (2010). Incidence and diagnostic diversity in first-episode psychosis. *Acta Psychiatrica Scandinavica*, *121*(4), 315-319.

Regier, D. A. (2007). Dimensional approaches to psychiatric classification: refining the research agenda for DSM-V: an introduction. *International Journal of Methods in Psychiatric Research*, *16*(S1), S1-S5.

Riecher-Rössler, A., & Rössler, W. (1998). The course of schizophrenic psychoses: what do we really know? A selective review from an epidemiological perspective. *European Archives Of Psychiatry And Clinical Neuroscience*, *248*(4), 189-202.

Rietkerk, T., Boks, M. P. M., Sommer, I. E., Liddle, P. F., Ophoff, R. A., & Kahn, R. S. (2008). The genetics of symptom dimensions of schizophrenia: review and meta-analysis. *Schizophrenia Research*, *102*(1), 197-205.

Rosen, J. L., Miller, T. J., D'Andrea, J. T., McGlashan, T. H., & Woods, S. W. (2006). Comorbid diagnoses in patients meeting criteria for the schizophrenia prodrome. *Schizophrenia Research*, *85*(1), 124-131.

Rosen, K., & Garety, P. (2005). Predicting recovery from schizophrenia: a retrospective comparison of characteristics at onset of people with single and multiple episodes. *Schizophrenia Bulletin*, *31*(3), 735-750.

Rosenman, S., Korten, A., Medway, J., & Evans, M. (2003). Dimensional vs. categorical diagnosis in psychosis. *Acta Psychiatrica Scandinavica*, *107*(5), 378-384.

Rwegellera, G. G. C. (1977). Psychiatric morbidity among West Africans and West Indians living in London. *Psychological Medicine*, *7*(02), 317-329.

Saha, S., Chant, D., Welham, J., & McGrath, J. (2005). A systematic review of the prevalence of schizophrenia. *PLoS Medicine*, *2*(5), e141.

Salokangas, R. (2003). Symptom dimensions and outcome in schizophrenia. *World Psychiatry*, *2*(3), 172.

Samer, J., & Yamout, R. (2012). *Public health in the Arab world.* Cambridge, UK: Cambridge University Press.

Sariaslan, A., Larsson, H., D'Onofrio, B., Långström, N., Fazel, S., & Lichtenstein, P. (2014). Does population density and neighborhood deprivation predict schizophrenia? A nationwide Swedish family-based study of 2.4 million individuals. *Schizophrenia Bulletin*, sbu105.

Sartorius, N., Jablensky, A., Korten, A., Ernberg, G., Anker, M., Cooper, J. E., & Day, R. (1986). Early manifestations and first-contact incidence of schizophrenia in different cultures: a preliminary report on the initial evaluation phase of the WHO Collaborative Study on determinants of outcome of severe mental disorders. *Psychological Medicine*, *16*(04), 909-928.

Sayed, S. M., Maghraby, M. M., Hafeiz, H. B., & Buckley, M. M. (1986). Psychiatric diagnostic categories in Saudi Arabia. *Acta Psychiatrica Scandinavica*, *74*(6), 553-554.

Saykin, A. J., Gur, R. C., Gur, R. E., Mozley, P. D., Mozley, L. H., Resnick, S. M., ... & Stafiniak, P. (1991). Neuropsychological function in schizophrenia: selective impairment in memory and learning. *Archives Of General Psychiatry*, *48*(7), 618-624.

Schneider, K. (1959) Clinical Psychopathology *(trans. M.W. Hamilton). New York: Grune and Stratton.*

Schwartz, D. T., & Mintz, N. L. (1963). Ecology and psychosis among Italians in 27 Boston communities. *Social Problems*, *10*(4), 371-374.

Selten, J. P., & Sijben, N. (1994). First admission rates for schizophrenia in immigrants to the Netherlands. *Social Psychiatry and Psychiatric Epidemiology*, *29*(2), 71-77.

Selten, J. P., Slaets, J. P. J., & Kahn, R. S. (1997). Schizophrenia in Surinamese and Dutch Antillean immigrants to The Netherlands: evidence of an increased incidence. *Psychological medicine*, *27*(04), 807-811.

Selten, J. P., Veen, N., Feller, W., Blom, J. D., Kahn, R., Schols, D., ... & Van Der Graaf, Y. O. L. A. N. D. A. (2001). Incidence of psychotic disorders in immigrant groups to The Netherlands. *The British Journal of Psychiatry*, *178*(4), 367-372.

Serretti, A., Macciardi, F., & Smeraldi, E. (1996). Identification of symptomatologic patterns common to major psychoses: proposal for a phenotype definition. *American journal of medical genetics*, *67*(4), 393-400.

Serretti, A., Rietschel, M., Lattuada, E., Krauss, H., Schulze, T. G., Müller, D. J., ... & Smeraldi, E. (2001). Major psychoses symptomatology: factor analysis of 2241 psychotic subjects. *European archives of psychiatry and clinical neuroscience*, *251*(4), 193-198.

Shalhoub-Kevorkian, N. (1999). Law, politics, and violence against women: A case study of Palestinians in Israel. *Law & Policy*, *21*(2), 189-211.

Shaltout, T., Bener, A., Al Abdullah, M., Al Mujalli, Z., & Shaltout, H. T. (2007). Acute and transient psychotic disorders in a rapidly developing country, State of Qatar. *Medicina (Kaunas)*, *43*(7), 7.

Sharifi, V., Kermani-Ranjbar, T., Amini, H., Alaghband-rad, J., Salesian, N., & Seddigh, A. (2009). Duration of untreated psychosis and pathways to care in patients with first-episode psychosis in Iran. *Early Intervention In Psychiatry*, *3*(2), 131-136.

Shaw, R. J., Atkin, K., Bécares, L., Albor, C. B., Stafford, M., Kiernan, K. E., ... & Pickett, K. E. (2012). Impact of ethnic density on adult mental disorders: narrative review. *The British Journal of Psychiatry*, *201*(1), 11-19.

Shergill, S. S., van Os, J., & Murray, R. M. (1999). Schizophrenia and depression: what is their relationship. *Managing the Depressive Symptoms of Schizophrenia*, 12-29.

Shrivastava, A., Shah, N., Johnston, M., Stitt, L., Thakar, M., & Chinnasamy, G. (2010). Effects of duration of untreated psychosis on long-term outcome of people

hospitalized with first episode schizophrenia. *Indian Journal Of Psychiatry*, *52*(2), 164.

Shtasel, D. L., Gur, R. E., Gallacher, F., Heimberg, C., & Gur, R. C. (1992). Gender differences in the clinical expression of schizophrenia. *Schizophrenia Research*, *7*(3), 225-231.

Singh, S. P., Cooper, J. E., Fisher, H. L., Tarrant, C. J., Lloyd, T., Banjo, J., ... & Jones, P. (2005). Determining the chronology and components of psychosis onset: The Nottingham Onset Schedule (NOS). *Schizophrenia research*, *80*(1), 117-130.

Sonmez, S., Apostopoulos, Y., Tran, D., & Rentrope, S. (2011). Human rights and health disparities for migrant workers in the UAE. *Health and Human Rights*, *13*(2),

Spitzer, R. L., Endicott, J., & Robins, E. (1978). Research diagnostic criteria: rationale and reliability. *Archives Of General Psychiatry*, *35*(6), 773-782.

StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP.

Stromgren, E.(1982) Development of concepts of schizophrenia. In handbook of psychiatry 3:psychoses of uncertain tetiology (eds J.K Wing & L.Wind) p. 17. Cambridge: Cambridge university press.

Struening, E. L., Perlick, D. A., Link, B. G., Hellman, F., Herman, D., & Sirey, J. A. (2001). Stigma as a barrier to recovery: The extent to which caregivers believe most people devalue consumers and their families. *Psychiatric Services*, *52*(12), 1633-1638.

Sundquist, K., & Ahlen, H. (2006). Neighbourhood income and mental health: a multilevel follow-up study of psychiatric hospital admissions among 4.5 million women and men. *Health & place*, *12*(4), 594-602.

Sundquist, K., Frank, G., & Sundquist, J. (2004). Urbanisation and incidence of psychosis and depression Follow-up study of 4.4 million women and men in Sweden. *The British Journal of Psychiatry*, *184*(4), 293-298.

Szymanski, S., Lieberman, J. A., Alvir, J. M., Mayerhoff, D., Loebel, A., Geisler, S., ... & Cooper, T. (1995). Gender differences in onset of illness, treatment response, course, and biologic indexes in first-episode schizophrenic patients. *American Journal of Psychiatry*, *152*(5), 698-703.

Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008). Schizophrenia,"just the facts" what we know in 2008. 2. Epidemiology and etiology. *Schizophrenia Research*, *102*(1), 1-18.

Taylor, B. M. A., & Abrams, R. (1978). The Prevalence ofSchizophrenia: A Reassessment Using Modern. *Am J Psychiatry*, *135*(8).

Test, M. A., Burke, S. S., & Wallisch, L. S. (1990). Gender differences of young adults with schizophrenic disorders in community care. *Schizophrenia Bulletin*, *16*(2), 331.

Thara, R. (2004). Twenty-year course of schizophrenia: the Madras Longitudinal Study. *Canadian Journal of Psychiatry*, *49*, 564-569.

Thomas, S. P., & Nandhra, H. S. (2009). Early intervention in psychosis: a retrospective analysis of clinical and social factors influencing duration of untreated psychosis. *Primary care companion to the Journal of clinical psychiatry*, *11*(5), 212.

Thornhill, J. T. (Ed.). (2011). *NMS Psychiatry*. Lippincott Williams & Wilkins.

Thornicroft, G. (2008). Stigma and discrimination limit access to mental health care. *Epidemiologia e psichiatria sociale*, *17*(01), 14-19.

Thorup, A., Petersen, L., Jeppesen, P., Ohlenschlæger, J., Christensen, T., Krarup, G., ... & Nordentoft, M. (2007). Gender differences in young adults with first-episode

schizophrenia spectrum disorders at baseline in the Danish OPUS study. *The Journal Of Nervous And Mental Disease*, *195*(5), 396-405.

Toomey, R., Kremen, W. S., Simpson, J. C., Samson, J. A., Seidman, L. J., Lyons, M. J., ... & Tsuang, M. T. (1997). Revisiting the factor structure for positive and negative symptoms: evidence from a large heterogeneous group of psychiatric patients. *American Journal of Psychiatry*, *154*(3), 371-377.

Tsuang, M. T., & Winokur, G. (1974). Criteria for subtyping schizophrenia: clinical differentiation of hebephrenic and paranoid schizophrenia. *Archives of General Psychiatry*, *31*(1), 43-47.

Turner, R. J., Dopkeen, L. S., & Labreche, G. P. (1970). Marital status and schizophrenia: A study of incidence and outcome. *Journal Of Abnormal Psychology*, *76*(1), 110.

Van Dael, F., Versmissen, D., Janssen, I., Myin-Germeys, I., van Os, J., & Krabbendam, L. (2006). Data gathering: biased in psychosis?. *Schizophrenia Bulletin*, *32*(2), 341-351.

van Os, J., & Verdoux, H. (2003). Diagnosis and classification of schizophrenia: categories versus dimensions, distributions versus disease. *The Epidemiology Of Schizophrenia*, 364-410.

Van Os, J., Castle, D. J., Takei, N., Der, G., & Murray, R. M. (1996). Psychotic illness in ethnic minorities: clarification from the 1991 census. *Psychological Medicine*, *26*(01), 203-208.

Van Os, J., Driessen, G., Gunther, N., & Delespaul, P. (2000). Neighbourhood variation in incidence of schizophrenia Evidence for person-environment interaction. *The British Journal of Psychiatry*, *176*(3), 243-248.

van Os, J., Gilvarry, C., Bale, R., Van Horn, E., Tattan, T., & White, I. (1999). A comparison of the utility of dimensional and categorical representations of psychosis. *Psychological medicine*, *29*(03), 595-606.

Van Os, J., Hanssen, M., Bak, M., Bijl, R. V., & Vollebergh, W. (2003). Do urbanicity and familial liability coparticipate in causing psychosis?. *American Journal of Psychiatry*, *160*(3), 477-482.

Van Os, J., Marcelis, M., Sham, P., Jones, P., Gilvarry, K., & Murray, R. (1997). Psychopathological syndromes and familial morbid risk of psychosis. *The British Journal of Psychiatry*, *170*(3), 241-246.

Vanasse, A., Courteau, J., Fleury, M. J., Grégoire, J. P., Lesage, A., & Moisan, J. (2012). Treatment prevalence and incidence of schizophrenia in Quebec using a population health services perspective: different algorithms, different estimates. *Social Psychiatry And Psychiatric Epidemiology*, *47*(4), 533-543.

Varma, V. K., Wig, N. N., Murthy, R. S., & Misra, A. K. (1980). Socio-demographic correlates of schizophrenia, affective psychoses and neuroses in a clinic in India. *Acta Psychiatrica Scandinavica*, *61*(5), 404-412.

Verdoux, H., Liraud, F., Bergey, C., Assens, F., Abalan, F., & van Os, J. (2001). Is the association between duration of untreated psychosis and outcome confounded? A two year follow-up study of first-admitted patients. *Schizophrenia research*, *49*(3), 231-241.

Verdoux, H., Van Os, J., Maurice-Tison, S., Gay, B., Salamon, R., & Bourgeois, M. (1998). Is early adulthood a critical developmental stage for psychosis proneness? A survey of delusional ideation in normal subjects. *Schizophrenia research*, *29*(3), 247-254.

Vogel, D. L., Wade, N. G., Wester, S. R., Larson, L., & Hackler, A. H. (2007). Seeking help from a mental health professional: The influence of one's social network. *Journal Of Clinical Psychology*, *63*(3), 233-245.

Watkins, F., & Jacoby, A. (2007). Is the rural idyll bad for your health? Stigma and exclusion in the English countryside. *Health & Place*, *13*(4), 851-864.

Weich, S., Twigg, L. I. Z., & Lewis, G. (2006). Rural/non-rural differences in rates of common mental disorders in Britain Prospective multilevel cohort study. *The British Journal of Psychiatry*, *188*(1), 51-57.

Weinberger, D., & Harrison, P. (2011) . Schizophrenia (3rd ed.) UK: Wiley-Blackwell.

Werbeloff, N., Drukker, M., Dohrenwend, B. P., Levav, I., Yoffe, R., van Os, J., ... & Weiser, M. (2012). Self-reported attenuated psychotic symptoms as forerunners of severe mental disorders later in life. *Archives of General Psychiatry*, *69*(5), 467-475.

Werner, S., Malaspina, D., & Rabinowitz, J. (2007). Socioeconomic status at birth is associated with risk of schizophrenia: population-based multilevel study. *Schizophrenia Bulletin*, *33*(6), 1373-1378.

Wessely, S., Castle, D., Der, G., & Murray, R. (1991). Schizophrenia and Afro-Caribbeans. A case-control study.

The British Journal of Psychiatry, *159*(6), 795-801.

Whitley, R., & McKenzie, K. (2005). Social capital and psychiatry: review of the literature. *Harvard review of psychiatry*, *13*(2), 71-84.

Wilson, J. V. (1996). Diseases of Babylon: an examination of selected texts. *Journal of the Royal Society of Medicine*, *89*(3), 135.

World Health Organisation (1979) Schizophrenia: An International follow-up study. Chichester, UK: John Wiley and Sons; 1979.

World Health Organisation (1993)The ICD-10 Classification of metal and Behavioural Disorders . Diagnostic Criteria for Research. World Health Organization ,Geneva

World Health Organization. (1992). The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines.

World Health Organization. (2004). *International statistical classification of diseases and related health problems* (Vol. 1). World Health Organization

Youssef, H. A., Youssef, F. A., & Dening, T. R. (1996). Evidence for the existence of schizophrenia in medieval Islamic society. *History of Psychiatry*, *7*(25), 055-62.

Zarroug, E. T. A. (1975). The frequency of visual hallucinations in schizophrenic patients in Saudi Arabia. *The British Journal of Psychiatry*, *127*(6), 553-555.

Zimmerman, F. J., & Katon, W. (2005). Socioeconomic status, depression disparities, and financial strain: what lies behind the income-depression relationship?. *Health Economics*, *14*(12), 1197-1215.

Zolkowska, K., Cantor-Graae, E., & McNeil, T. F. (2001). Increased rates of psychosis among immigrants to Sweden: is migration a risk factor for psychosis?. *Psychological Medicine*, *31*(04), 669-678.

Züchner, S., Roberts, S. T., Speer, M. C., & Beckham, J. C. (2007). Update on psychiatric genetics. *Genetics in Medicine*, *9*(6), 332-340.

APPENDIX 1

DOCUMENTS RELEVANT TO RIYADH AREAS, DISTRICTS AND NEIGHBOURHOODS

Riyadh by areas, districts and neighbourhoods

Areas	Districts	Neighbourhoods
1: NORTH RIYADH	**1: Al-Shmal**	1: Al-Rabeea 2: Al-Nada 3: Al-shafa 4: Al-Narjes 5: Al-ared 6: Al-Nafl 7: Al-Ageg 8: Al-Wadi 9: Al-Ghadeer 10: Al-Yasmeen 11: Al-Flah 12: Al-Gerwan 13: Hteen 14: Almalga 15: King Mohammed Un
	2: Al-Dereyah	16: Al-Dereyah

2: EAST RIYADH	**3: Al-Rodah**	17: Al-Rodah 18: Al-Gods 19: Al-Hamra 20: Qortba 21: Al-Andlos 22: King Faisal
		23: Gornata 24: Al-Nahda 25: Al-Kaleej 26: Ashbelya 27: Alyarmook 28: Al-Monsyah 29: Al-Mozlyah 30: Alrmal 31: Al-Jnadrya
	4: Al-Naseem	32: Al-Rayan 33: Al-Rwabi 34: Al-Mnar 35: Al-Slam 36: Al-Naseem 37: Al-Natheem 38: Al-Rmayah 39: Al-Saadah

	5: Alslay	40: Al-Fayha 41: Al-Jazerah 42: Al-Sly 43: Al-Noor 44: Al-Mnach 45: Al-Dfeaa 46: Al-Eskan 47: New senaayah 48: Kashm alaan
3: WEST RIYADH	**6: Erga**	49: Tweeg 50: Al-Kozama 51: Lbn 52: Erga 53: Almhdya
	7: Nmar	54: Thrt Lbn 55: Thrt Nmar 56: Nmar 57: Alhazm 58: Derab

	8: Al-Oreja	59: Wadi Lbn 60: Al-Oreja 61: Middle Oreja 62: Shabra 63: West Al-Swedi 64: Thrt Al-Bdeaa 65: Sltana 66: Al-Zahra 67: Al-Swedi 68: West Oreja
4: SOUTH RIYADH	**9: Al-Azezyah**	69: Al-Dar albedah 70: Al-Azezyah 71: Almnsoryah 72: Almsfat 73: Tebah
	10: Al-Shfa	74: Ahad
		75: Al-Marwah 76: Okath 77: Al-Shfa 78: Bdr 79: Almsana
	11: Al-Hayer	80: Al-Hayer

5: CENTRAL RIYADH	**12: Al-Olyah**	81: Al-Olyah 82: Al-Slemanyah 83: Al-Wrood 84: Al-Mgrzat 85: Slah aldeen 86: Al-Waha 87: Al-Ezdhar 88: Al-Nzha 89: Al-Mrooj 90: Al-Mrslat 91: King Fahd 92: Al-Tawn 93: Al-Mseef 94: King Abdullah 95: King Abdulazez 96: Altakasosi
	13: Al-Mather	97: North Mather 98: Al-Rhmanyah 99: Al-Mhamdyah 100: Al-Nakeel 101: Al-Raed 102: West Um Alhmam 103: King Saud Un

	14: Al-Malz	104: Jarer 105: Al-Rabwah 106: Al-zhra 107: Al-sfa 108: Al-dobat 109: Al-malz 110: Al-Fotah 111: Al-Mraba 112: Al-Snaaya 113: Alfarog 114: Al-Wzarat 115: Thleem 116: Al-Amal
	15: Al-Shmesi	117: Al-Rafeea 118: Al-Hada 119: Al-Shrfya 120: Al-nasryah 121: Syah 122: Al-Washm

		123: Al-Nmothjyah 124: Al-Motmrat 125: Al-Badea 126: Um-Sleem 127: Al-Shmesi 128: Al-Jradyah 129: Al-Fakryah 130: Olesha 131: Um-Alhmam
	16: Al-Batha	132: Al-Ymamh 133: Al-Oud 134: Al-Khaldyah 135: Al-Mansorah 136: Manfoha 137: Makal 138: Al-Jabra 139: Al-Waseta 140: Al-Dobyah 141: Gbera 142: Slam 143: Al-Salhyah 144: Al-Fayslyah 145: Otega 146: Al-Margb 147: Al-Derah 148: Skrnyah

		149: Al-Batha 150: Al-Gra
6: DIPLOMATIC QUARTER		151: Diplomatic quarter

APPENDIX 2
DOCUMENTS RELEVENT TO THE ETHICAL CONSIDERATION

Research Ethics Office

5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London SE1 9NH
Tel 020 7848 4077/4070/4020
Email rec@kcl.ac.uk
www.kcl.ac.uk/research/ethics

KING'S College LONDON

Hanan Al Fayez
10 Rushmore House
73 Russal Road
London
W14 8HW

10 May 2012

Dear Hanan Al Fayez

PNM/11/12-62 A cross-cultural examination of variability and predictors of incidence of schizophrenia in Riyadh versus London.

Review Outcome: Full Approval

Thank you for sending in the amendments/clarifications requested to the above project. I am pleased to inform you that these meet the requirements of the PNM RESC and therefore that full approval is now granted.

Please ensure that you follow all relevant guidance as laid out in the King's College London Guidelines on Good Practice in Academic Research (http://www.kcl.ac.uk/college/policyzone/index.php?id=247).

For your information ethical approval is granted until **10 May 2015**. If you need approval beyond this point you will need to apply for an extension to approval at least two weeks prior to this explaining why the extension is needed, (please note however that a full re-application will not be necessary unless the protocol has changed). You should also note that if your approval is for one year, you will not be sent a reminder when it is due to lapse.

Ethical approval is required to cover the duration of the research study, up to the conclusion of the research. The conclusion of the research is defined as the final date or event detailed in the study description section of your approved application form (usually the end of data collection when all work with human participants will have been completed), not the completion of data analysis or publication of the results. For projects that only involve the further analysis of pre-existing data, approval must cover any period during which the researcher will be accessing or evaluating individual sensitive and/or un-anonymised records. Note that after the point at which ethical approval for your study is no longer required due to the study being complete (as per the above definitions), you will still need to ensure all research data/records management and storage procedures agreed to as part of your application are adhered to and carried out accordingly.

If you do not start the project within three months of this letter please contact the Research Ethics Office.

Should you wish to make a modification to the project or request an extension to approval you will need approval for this and should follow the guidance relating to modifying approved applications: http://www.kcl.ac.uk/innovation/research/support/ethics/applications/modifications.aspx
The circumstances where modification requests are required include the addition/removal of participant groups, additions/removal/changes to research methods, asking for additional data from participants, extensions to the ethical approval period. Any proposed modifications should only be carried out once

full approval for the modification request has been granted.

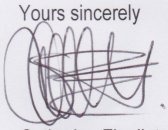
Any unforeseen ethical problems arising during the course of the project should be reported to the approving committee/panel. In the event of an untoward event or an adverse reaction a full report must be made to the Chair of the approving committee/review panel within one week of the incident.

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact your panel/committee administrator in the first instance (http://www.kcl.ac.uk/innovation/research/support/ethics/contact.aspx). We wish you every success with this work.

With best wishes

Yours sincerely



Catherine Fieulleteau
Senior Research Ethics Officer

Cc: Dr Jane Boydell

وزارة الصحة
Ministry of Health

KFSH-D Institutional Review Board (IRB)
National Registration Number (H-05-D-002)
Federal Wide Assurance (00018714)
IRB Number (IRB00008686)

IRB Approval Letter
15 September 2012
IRB No.: IRB-079

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Institute of Psychiatry
alfayezhanan@gmail.com

Re: An Epidemiological study of variables and predictors of incidence of Schizophrenia in Riyadh, Saudi Arabia
Version number/Date: v2 / 15-sep-2012
Study Number: EXT034

Dear Ms. Hanan,

On 8 September 2012, the Institutional Review Board (IRB) at KFSH-D received your study documents for initial review. On 15 September 2012, the IRB reviewer reviewed the documents and suggested minor modifications. On 15 September 2012, updated documents were received and accepted by the IRB reviewer. The IRB approves the study documents in versions listed below.

The study is approved.

- If there are any amendments, please complete the "Amendments Submission From" and return it to the IRB. Amendments may not be initiated until IRB approval has been obtained.
- Upon study completion, we would be grateful if you would submit a final report.

If you have any further enquiries regarding the IRB's decision, you may contact the IRB Coordinator at Jamhawilo@kfsh.med.sa

IRB action type	☐ Full ☐ Expedited ☒ Exempt
Protocol	v2 / 15-sep-2012
Patient Information Sheet	v2 / 15-sep-2012
OPCRIT for Windows (v4), Item Checklist	v2 / 15-sep-2012
Number of subjects approved for your site	500

We thank you for submitting your study for review by the IRB at KFSH-D and wish you all the best with this study.

Khalid Akkari, MRCP
IRB Chairman
KFSH-D
1-2

Mohamed Sager, MD
Director, Research Administration
KFSH-D

Issued by IRB Coordinator: Lama Jamhawi, M.Sc.
Telephone: +966-3-8431111 Ext: 6808
Email: Jamhawilo@kfsh.med.sa

مستشفى الملك فهد التخصصي بالدمام
King Fahd Specialist Hospital-Dammam

Elements of the IRB Approval Letter

1. **Protocol and Consent Versions:** lists the major documents that have been approved by the IRB
2. **Recruitment Demographics:** Information showing the distribution of enrollment (in accordance with the Belmont Report's principle of Justice)
3. **Number of Subjects** – The maximum allowable number of subjects to be enrolled at each site. Any increase in this number must be approved by the IRB first.

Conditions of Approval

1. There are six conditions attached to approval letters:

   a. No subjects may be included in a study procedure prior to the first patient in (FPI) as specified in the protocol. This means that nothing can be done with subjects until after the date of the FPI.
   b. All unanticipated or serious adverse events must be reported to the IRB within 5 days.
   c. All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk. This includes any change of investigator, or site address.
   d. Inform the IRB prior to making prospective changes to the study procedures. If you know something will change, the IRB should also know.
   e. All protocol deviations must be reported to the IRB within 5 working days.
   f. All recruitment materials and methods must be approved by the IRB prior to being used, as these would be considered modifications.

Khalid Akkari, MRCP
IRB Chairman
KFSH-D

Mohamed Sager, MD
Director, Research Administration
KFSH-D

Issued by IRB Coordinator: **Lama Jambawi, M.Sc.**
Telephone +966-1-8431111 **Ext** 6808
Email: Jambawilo@kfsh.med.sa

PRINCE SULTAN MILITARY MEDICAL CITY
P.O. Box 7897, Riyadh 11159
Kingdom of Saudi Arabia

Research Ethics Committee

30 December 2012

MS. HANAN AL FAYEZ

Re: An epidemiological study of variables and predictors of incidence of schizophrenia in Riyadh, Saudi Arabia

Dear Ms. Hanan Al Fayez,

Please be informed that the abovementioned proposal has been approved by the Research Ethics Committee as chairman action with no cost to PSMMC.

Your research protocol has been documented under:

Project No.	487
Date Approved	29 December
Series of	2012

Kindly quote the project number indicated herein in all transactions and communications. You are advised to submit a report in relation to this research scheme to update the committee of its progress.

I trust your research scheme proves fruitful and beneficial to the PSMMC.

Best regards

PP. Abdel

DR. SAEED KADASAH
Chairman, Research Ethics Committee
First Floor, Building (15) 136

Health Affairs Executive Office | File # 11167/2012
10/11/2012 14:38 | 11167/2012

Kingdom of Saudi Arabia
National Guard Health Affairs

المملكة العربية السعودية
الحرس الوطني - الشؤون الصحية

Institutional Review Board 14572 1515 14571 irb@ngha.med.sa

MEMORANDUM

Ref. #: IRBC/287/12

Date: **(G) 07 NOVEMBER 2012**
(H) 22 Thul-Hijjah 1433

To: **MS. HANAN AL FAYEZ**
PhD Student
Institute of Psychiatry
Kings College London

Subject: **PROTOCOL RC12/039 - "An Epidemiological Study of Variables and Predictors of Incidence of Schizophrenia in Riyadh Saudi Arabia"**

This is in reference to your subject proposal, which has been reviewed by the IRB Office on the 5th of November 2012 through the expedited review process. Upon recommendation of the Research Committee, and following the review of the IRB on the ethical aspects of the proposal, you are granted permission to conduct your study.

Your research proposal is **approved for one year** commencing from the above date with the following conditions:

TERMS OF APPROVAL:

1. **Annual Reports**: Continued approval of this project is dependent on the submission of an Annual Report. Please provide KAIMRC with an Annual Report **determined by the date of your letter of approval**.
2. **Amendments to the approved project**: Changes to any aspect of the project require the submission of a Request for Amendment to KAIMRC and must not begin without an approval from KAIMRC. Substantial variations may require a new application.
3. **Future correspondence**: Please quote the project number and project title above in any further correspondence.
4. **Monitoring**: Projects may be subject to an audit or any other form of monitoring by KAIMRC at any time.
5. **Retention and storage of data**: The PI is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

Prof. Amin Kashmeery
Chairman, Institutional Review Board (IRB)
National Guard Health Affairs

Dr. Mohammed Al Jumah
Executive Director, KAIMRC
National Guard Health Affairs

Dr. Bandar Al Knawy
Chief Executive Officer
National Guard Health Affairs

AK/AS/jue

P.O. Box 22490, Riyadh 11426
Tel. 8011111
Telex : 403450 NGRMED SJ
KFH - MATERIALS 14574 (.05/96) (ORACLE 29795)

ص.ب. ٢٢٤٩٠ الرياض ١١٤٢٦
تلفون: ٨٠١١١١١
تلكس ٤٠٣٤٥٠

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

DEPARTMENT OF MENTAL HEALTH

MBC 93, Fax 38957, Phone 36357

Internal Memorandum

TO: **Saleh Al Mofada, MD**
Executive Director
Medical and Clinical Affairs

DATE: 24 Muharram 1434
8 December 2012

FROM: **Mohammad Ghaziuddin, MD**
Chairman
Department of Mental Health

8/12/12.

REF: PSY: 006-34

SUBJECT: OPINION REGARDING DATA COLLECTION FROM SAUDI HOSPITAL.

I am writing to support the request of Ms. Hanan Alfayez to obtain data from the hospital examining the predictors and variables of incidence of schizophrenia in the Kingdom. This is a project that will increase awareness of this disabling condition.

The Department of Mental Health will cooperate fully with Ms. Hanan in her efforts.

Thank you.

cc: Abdulrahman Alrajhi, MD, Executive Director, Academic and Training Affairs

بسم الله الرحمن الرحيم

Kingdom of Saudi Arabia
Ministry of Higher Education
King Saud University
Code 034
College of Education

المملكة العربية السعودية
وزارة التعليم العالي
جامعة الملك سعود
رمزها ٠٣٤
كلية التربية

Date: ١٤٣٤/١/١٠ التاريخ: No.: ٣/٨/١١٥٠٤٧ الرقم:

سعادة المدير الطبي بمستشفى الملك خالد الجامعي حفظه الله

السلام عليكم ورحمة الله وبركاته وبعد :-

أود افادتكم بأن مبتعثة القسم لدراسة الدكتوراه / حنان بنت محمد الفايز تقوم بإعداد بحث لإتمام مرحلة الدكتوراه ويستلزم الأمر تطبيق أداة بحثها على ملفات بعض من مراجعي ومراجعات العيادات الخارجية والمنومين بالمستشفى.

نأمل تسهيل مهمتها شاكرين ومقدرين تعاونكم...

وتقبلوا خالص تحياتي ،،،

رئيس قسم علم النفس
١٤٣٤/م/١٠
ا.د.فهد بن عبدالله الدليم

.ناصر

سعادة مدير ادارة الملفات تسهيل عمل د/حنان حسب النظام وشكرا
مدير مركز الطب النفسي بالنيابة د/عبدالله السبتي

بسم الله الرحمن الرحيم

المملكة العربية السعودية
وزارة الصحة
الإدارة العامة للبحوث والدراسات

الموضوع: تسهيل مهمة طالبة الدكتوراة/ حنان الفايز

سعادة / المشرف العام على مدينةالملك سعود الطبية **المحترم**

السلام عليكم ورحمة الله وبركاته،،،

إشارة إلى موضوع دراسة الطالبة / حنان بنت محمد علي الفايز، رقم السجل المدنى (١٠٣٠٠٤٥٠١٥) لدراسة مرحلة الدكتوراة فى تخصص الأمراض الذهانية – معهد الطب النفسي بجامعة كنجز كولدج- لندن ، رقم الطالبة الأكاديمى (١٠١٨٦٧٨/١)، وعنوان الرسالة :

"دراسة وبائية عن المتغيرات والتنبؤات في إنتشار مرض الفصام في مدينة الرياض، المملكة العربية السعودية"

"An Epidemiological study of variabiles and predictors of incidence of Schizophrenia in Riyadh, Saudi Arabia"

وقد إستوفت المذكورة كافة المستندات المطلوبة، وتمت مراجعتها من قبل اللجان المعنية ، وتمت الموافقة على تسهيل مهمة إجراء هذا البحث.

وحيث أن المذكورة عاليه ستنفذ دراستها فى مجمع الملك سعود الطبي ، نأمل من سعادتكم تسهيل مهمتها لجمع البيانات اللازمة بما يضمن أن لا يكون هناك أي تأثير على خدمة المراجعين والمرضى خلال قيامها بمهام بحثها، مع العلم بأن وزارة الصحة لا تتحمل أية أعباء مالية أو إدارية فى البحث.

شاكرين لكم حسن تعاونكم.

ولكم أطيب تحياتـــي ،،،

بسم الله الرحمن الرحيم

المملكة العربية السعودية
وزارة الصحة
الإدارة العامة للبحوث والدراسات

الموضوع: تسهيل مهمة طالبة الدكتوراة/ حنان الفايز

سعادة /مدير عام الشؤون الصحية بمنطقة الرياض **المحترم**

السلام عليكم ورحمة الله وبركاته،،،

إشارة إلى موضوع دراسة الطالبة / حنان بنت محمد علي الفايز، رقم السجل المدنى (١٠٣٠٠٤٥٠١٥) لدراسة مرحلة الدكتوراة فى تخصص الأمراض الذهانية – معهد الطب النفسي بجامعة كنجز كولدج- لندن ، رقم الطالبة الأكاديمى (١٠١٨٦٧٨/١)، وعنوان الرسالة :

"دراسة وبائية عن المتغيرات والتنبؤات في إنتشار مرض الفصام في مدينة الرياض، المملكة العربية السعودية"

"An Epidemiological study of variabiles and predictors of incidence of Schizophrenia in Riyadh, Saudi Arabia"

وقد إستوفت المذكورة كافة المستندات المطلوبة، وتمت مراجعتها من قبل اللجان المعنية ، وتمت الموافقة على تسهيل مهمة إجراء هذا البحث.

وحيث أن المذكورة عاليه ستنفذ دراستها فى مجمع الأمل للصحة النفسية بالرياض، نأمل من سعادتكم تسهيل مهمتها لجمع البيانات اللازمة بما يضمن أن لا يكون هناك أي تأثير على خدمة المراجعين والمرضى خلال قيامها بمهام بحثها، مع العلم بأن وزارة الصحة لا تتحمل أية أعباء مالية أو إدارية فى البحث.

شاكرين لكم حسن تعاونكم.

ولكم أطيب تحياتـــي ،،،

الإدارة العامة للبحوث والدراسات

APPENDIX 3
DOCUMENTS RELEVENT TO THE STUDY ASSESSMENTS

PATIENT INFORMATION SHEET

Hospital / patient information

Hospital name: ……

Hospital type : ☐MOH ☐Military ☐Non-military

ICD-9 code :.....

Case number : ……..

ICD-10 code…….

Patient file number:……

Date first contact : d/ ……. m/ ……. ☐2009 ☐2010

Patient type : ☐ In-patient ☐out-patient

Demographic Factors

Nationality : ☐Saudi ☐Non-Saudi (specify).....

Gender : ☐ Male ☐ Female

Age (when contact) ..... Date .....

Age (first onset) ..... Date .....

Place of residence Riyadh District ..... Neighbourhood .....

Place of origin .....

Religion .....

Employment ☐ Yes (specify)..... ☐No

Education ☐ Illiterate ☐ primary school ☐ secondary school ☐ High school ☐ university ☐Higer education

Marital status ☐Marred ☐Single ☐divorced ☐ separated ☐widow

If married number of children .....

Number of family member ☐less than 4 ☐between 4-8 ☐more than 8

Living status ☐ with his/her family ☐ with his/her family in low ☐Alone ☐Juvenile correctional Facility ☐Prison

Monthly income ☐less than 8000SR/month ☐between 8000-16000 SR ☐ more than 16000 SR

Psychiatric History

Source of information ☐patient ☐member of the family (specify)…… ☐ other

Reasons for consultation .....

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Early manifestation of the illness .....
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Alcohol use ☐Yes ☐ No
Drugs use ☐ Yes (specify) ..... ☐No
Any medical history.....
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……..
……
……

Family History

Family (Parents and siblings)

Members	Age	Education	Occupation	Relation	Any health problem	Comment
Father						
Mother						

Family (spouse and children)

Members	Age	Education	Occupation	Relation	Any health problem	Comment

Premorbid personality .....
……
……
……..

Stress pre onset ☐yes (specify) .....
☐No

<u>Pathway to care</u>

Where did the patient go first for help ?

☐Psychiatrist / Mental health professional (such as Neurologist)
☐Clinical psychologist
☐GP/Medical specialist (Non-Psychiatric)
☐Nurse/other Health workers/ social workers
☐Police
☐Traditional healer/ Other religious person
☐Other

Opcrit for Windows (v4), Item Checklist.

Details & History

1	Source of Rating	(1-6)	
2	Time Frame	(1-4)	
3	Gender	(0,1)	
4	Age of onset		
5	Mode of onset	(1-5)	
6	Single '(subject never married / lived as married)'	(0,1)	
7	Unemployed at onset	(0,1)	
8	Duration of illness in weeks (max=99)		
9	Poor work adjustment	(0,1)	
10	Poor premorbid social adjustment	(0,1)	
11	Premorbid personality disorder	(0,1)	
12	Alcohol/drug abuse within one year of onset of psychotic symptoms	(0,1)	
13	Family history of schizophrenia	(0,1)	
14	Family history of other psychiatric disorder	(0,1)	
15	Coarse brain disease prior to onset	(0,1)	
16	Definite psychosocial stressor prior to onset	(0,1)	

Appearance & Behaviour

17	Bizarre behaviour	(0,1)	
18	Catatonia	(0,1,2)	
19	Excessive activity	(0,1,2,3)	
20	Reckless activity	(0,1,2,3)	
21	Distractibility	(0,1,2,3)	
22	Reduced need for sleep	(0,1,2,3)	
23	Agitated activity	(0,1,2,3)	
24	Slowed activity	(0,1,2,3)	
25	Loss of energy/tiredness	(0,1,2,3)	

Speech & Form of Thought

26	Speech difficult to understand	(0,1)	
27	Incoherent	(0,1,2)	
28	Positive formal thought disorder	(0,1,2)	
29	Negative formal thought disorder	(0,1,2)	
30	Pressured speech	(0,1,2,3)	
31	Thoughts racing	(0,1,2,3)	

Affect and Associated Features

32	Restricted affect	(0,1,2)	
33	Blunted affect	(0,1,2)	
34	Inappropriate affect	(0,1,2)	
35	Elevated mood	(0,1,2,3)	
36	Irritable mood	(0,1,2,3)	
37	Dysphoria	(0,1,2,3)	
38	Diurnal variation (mood worse mornings)	(0,1)	
39	Loss of pleasure	(0,1,2,3)	
40	Altered libido	(0,1,2)	
41	Poor concentration	(0,1,2,3)	
42	Excessive self reproach	(0,1,2,3)	
43	Suicidal ideation	(0,1,2,3)	
44	Initial insomnia	(0,1,2,3)	
45	Middle insomnia (broken sleep)	(0,1)	
46	Early morning waking	(0,1,2,3)	
47	Excessive sleep	(0,1,2,3)	
48	Poor appetite	(0,1,2,3)	
49	Weight loss	(0,1,2,3)	
50	Increased appetite	(0,1,2,3)	
51	Weight gain	(0,1,2,3)	
52	Relationship between psychotic and affective symptoms	(0,1,2,3)	
53	Increased sociability	(0,1,2,3)	

Abnormal Beliefs and Ideas

54	Persecutory delusions	(0,1,2)	
55	Well organised delusions	(0,1,2)	
56	Increased self esteem	(0,1,2,3)	
57	Grandiose delusions	(0,1,2,3)	
58	Delusions of influence	(0,1,2)	
59	Bizarre delusions	(0,1,2)	
60	Widespread delusions	(0,1,2)	
61	Delusions of passivity	(0,1,2)	
62	Primary delusional perception	(0,1,2)	
63	Other primary delusions	(0,1,2)	
64	Delusions & hallucinations last for one week	(0,1,2)	
65	Persecutory/jealous delusions & hallucinations	(0,1,2)	
66	Thought insertion	(0,1,2)	
67	Thought withdrawal	(0,1,2)	
68	Thought broadcast	(0,1,2)	
69	Delusions of guilt	(0,1,2,3)	
70	Delusions of poverty	(0,1,2,3)	
71	Nihilistic delusions	(0,1,2,3)	

Abnormal Perceptions

72	Thought echo	(0,1,2)	
73	Third person auditory hallucinations	(0,1,2)	
74	Running commentary voices	(0,1,2)	
75	Abusive/accusatory/persecutory voices	(0,1,2)	
76	Other (non affective) auditory hallucinations	(0,1,2)	
77	Non-affective hallucination in any modality	(0,1,2)	

Substance Abuse or Dependence

78	Life time diagnosis of alcohol abuse/dependence	(0,1)
79	Life time diagnosis of cannabis abuse/dependence	(0,1)
80	Life time diagnosis of other abuse/dependence	(0,1)
81	Alcohol abuse/dependence with psychopathology	(0,1)
82	Cannabis abuse/dependence with psychopathology	(0,1)
83	Other abuse/dependence with psychopathology	(0,1)

General Appraisal

84	Information not credible	(0,1)
85	Lack of insight	(0,1)
86	Rapport difficult	(0,1)
87	Impairment/incapacity during disorder	(0,1,2,3)
88	Deterioration from premorbid level of functioning	(0,1)
89	Psychotic symptoms respond to neuroleptics	(0,1)
90	Course of disorder	(1-5)

APPENDIX 4
DOCUMENTS RELEVENT TO THE PUPLISHED PAPER
DURATION OF UNTREATED PSYCHOSIS AND PATHWAY TO CARE IN RIYADH, SAUDI ARABIA

Early Intervention IN PSYCHIATRY
First Impact Factor released in June 2010 and now listed in MEDLINE!
Early Intervention in Psychiatry 2015; : –
doi:10.1111/eip.12214

Original Article

Duration of untreated psychosis and pathway to care in Riyadh, Saudi Arabia

Hanan Al Fayez, Julia Lappin, Robin Murray and Jane Boydell

Abstract

Aim: Recent studies of 'duration of untreated psychosis' (DUP) indicate that some patients remain untreated in the community for some time. Considerable emphasis has been placed on reducing the DUP. However, most studies investigating DUP have been conducted in Western countries, where well-developed primary care systems are available. This study aims to describe DUP and its association with both demographic factors and pathways to care in Riyadh, Saudi Arabia.

Methods: A retrospective study of 421 new case records of all Saudi schizophrenia patients over a 2-year period in six governmental hospitals in Riyadh, Saudi Arabia.

Results: The median DUP was 1.41 years (interquartile range 0.35–2.81 years). The longest time to contact was 9.86 years but 90% had a DUP shorter than 5 years. Older age at onset, single marital status and higher educational level were associated with shorter DUP. Long DUP was associated with help seeking from traditional healers.

Conclusion: In Saudi Arabia, it usually takes longer for patients to seek help from psychiatric services after their first psychosis onset than it does in Western countries. The results suggest that the DUP is influenced by both demographic factors and pathways to care.

Institute of Psychiatry, Psychosis Studies, King's College London, London, UK

Corresponding author: Ms. Hanan Al Fayez. Institute of psychiatry. Psychosis Studies. King's College London. DeCrespigny Park, Camberwell. London SE5 8AF, UK.
Email: hanan.alfayez@kcl.ac.uk

Received 16 July 2014; accepted 9 November 2014

Key words: duration of untreated psychosis, pathway to care, schizophrenia.

INTRODUCTION

The difference between the time that patients present for psychiatric care and the time that they had their first episode of schizophrenia is termed 'duration of untreated psychosis' (DUP). Studies of DUP have indicated that some patients remain untreated in the community for 1–2 years[1–3] More recent studies have indicated a shorter DUP: 44.6,[4] 18.6[5] and 11 weeks.[6] This later study was based in the UK cities. Most studies have been conducted in Western countries, where well-developed primary care systems are available. It is unclear how generalizable such findings may be to countries with less developed psychiatric services, and few studies to date have been conducted in developing countries. One such study that compared DUP, in Egyptian and Saudi patients, with first-episode psychosis, explored the socio-demographic, clinical and help-seeking characteristics between the two samples. The mean DUP did not significantly differ (3.2 years Egyptian; 3.1 years Saudis).[7]

Sharifi and co-workers conducted a study of first-episode psychosis (FEP) in patients in Iran and, unexpectedly, found that the median DUP was 11 weeks, thus comparable to that found in Western studies. Similar proportions of patients initially sought help from psychiatrists (n = 23, 25.3%) as from traditional healers (n = 21, 23.1%), with a smaller proportion seeking help first from a general practioner (n = 16, 17.6%).[8]

Causal attributions, pathway to care and clinical features were examined in a sample of 54 first-episode psychosis patients in South Africa to test if there were associations between these factors and DUP. The results showed that both spiritual attributions of cause (49% of patients) and a previous consultation with a traditional healer (39% of patients)

were associated with long DUP.[9] Another study was conducted in Karachi, Pakistan, and showed that because of the lack of a primary care system, most of the psychotic patients contacted psychiatrists directly.[10] Understanding the importance of early diagnosis and treatment is an important step to eliminate this delay and mitigate its impact on the prognosis of the disease. The first stage of help seeking is the decision to seek help and this is what seems to be prone to most delay.[11,12] The decision is influenced by a large number of factors, perhaps the most important of which are cultural.[13] In Saudi society, the delay that occurs before seeking help could be potentially understood as due to the belief that supernatural powers such as magic are the cause of these symptoms.[14]

The main aim of this study is to describe the DUP in the capital city of Saudi Arabia. The secondary aim is to identify any associations between DUP and both patient demographic factors (nationality, age, gender, income, marital status, living status (i.e. living with family, living alone and other), family size, education level, employment status, monthly income, history of drug abuse) and their first pathway to care (non-psychiatric and psychiatric health profession – traditional healer/other religious person).

METHODS

A descriptive and analytical study utilizing retrospective evaluation of 421 new cases of psychosis patient records (in- and outpatients) from all governmental hospitals in Riyadh, Saudi Arabia. The city of Riyadh is served by a number of Ministry of Health (MOH) hospitals and other governmental hospitals that provide psychiatric services. Hospitals included in this study were as follows: The Amal Complex for Mental Health, King Abdulaziz Medical City, Prince Sultan Military Medical City, King Saud Medical City, King Faisal Specialist Hospital & Research Centre, and King Khalid University Hospital. This provided comprehensive coverage of all inpatients and almost all outpatients undergoing treatment for psychosis in Riyadh. Inclusion criteria were as follows: all psychotic patients who did not have an organic psychotic illness (based upon ICD-10 (10th revision of the International Statistical Classification of Diseases and Related Health Problem)), age at onset from 16 up to 65 years, residents of Riyadh city, no previous contact with any psychiatric services and Saudi nationality. The age range was chosen to reflect clinical practice. From a total of 425 patients satisfying the inclusion criteria, 4 patients were excluded due to poor quality information, giving a total sample of n = 421. There were neither dropouts nor censorings due to the nature of the study design. Among the 421 patients, 211 records had date of onset given by day and 210 patients had date of onset given by month so an approximated date of 1st of each month was substituted. Therefore, the maximum discrepancy from a true value could have been 0.083 year (= 30 days). For the endpoint, all records recorded the day.

Ethical approval for this study was granted by both Kings College London and the Institutional Review Board (IRB) of the Ministry of Health (MOH) Saudi Arabia. Approval to undertake this study and collect full demographic and diagnostic data from patients' medical files was also granted by all of the hospitals included in the study.

Sample

Clinical and demographic data on all people from Riyadh city, who presented with psychosis between 2009 and 2011, were collected. We identified cases by generating a list of all patients from computer records in each hospital included in the study from 2009. ICD-10 codes F20-F29 and F30-F32[15] were used to initially identify cases. Demographic factors and pathway to care were collected from patient records (nationality, age, gender, income, marital status, living status (i.e. living with family, living alone and other), family size, education level, employment status, monthly income, history of drug abuse and the treatment-seeking behaviours).

Diagnostic procedure

Only true incident cases were included in this study (had never contacted psychiatric services anywhere), and then all case notes were rated using the Operational Criteria (OPCRIT) checklist by the main researcher to determine ICD-10 schizophrenia diagnoses using the associated computer program.

Duration of untreated psychosis

Information was extracted from all the psychiatric records in order to verify the date of the onset of symptoms and treatment, pathway to care and sociodemographic variables. Onset of psychosis was defined as the presence of one of the following psychotic symptoms for 1 week or more: delusions; hallucinations; thought disorder; and bizarre, grossly inappropriate and/or disorganized behaviour with a noticeable deterioration in function. Following previous studies,[6,16] the endpoint of DUP in this

study was considered as the date of first contact with mental health services whether they were admitted to hospital or only treated as outpatients.

Statistical analysis

Comparisons between groups in the sample were conducted using the chi-squared test and the Wilcoxon rank-sum test, as appropriate for the distribution of the data. The DUP was defined as the period in days from the onset of positive psychotic symptoms until the start of psychiatric treatment. As noted in several other studies and also for our sample, the DUP did not have a normal distribution and was heavily skewed. Even after log transformation, the distribution still showed non-normality. This and the observation that DUP is time to event data led to the choice of survival analysis as the best approach to analyse the relationship between DUP and other variables. The onset of psychosis as defined earlier was chosen as the entry point and contact with services was the endpoint. Specifically, tests for univariable associations between DUP and other variables were carried out using Kaplan–Meier survival curves. Log-rank tests and Wilcoxon tests were performed to assess differences between groups in the survival probability. The Wilcoxon rank-sum test was also conducted to compare DUP between groups. A P-value cut-off point of 0.25 was chosen to select variables to be examined in a Cox proportional hazard regression. A high P-value was chosen to avoid missing any potentially important variables in the multivariable model. For the purpose of statistical significance, however, P-values of <0.05 were chosen. The final model with the smallest AICc (second-order Akaike information criterion) was chosen as the smaller AICc indicates the better model among a set of Cox regression models. Unadjusted and adjusted hazard ratios (HRs) of predictors included in the final model are presented.

The assumption of proportional hazards was found not to be invalidated in the final model. An HR > 1.0 represents an increased risk of contact with services and hence indicates a shorter DUP.

All analyses were conducted using SAS (version 9.2; SAS Inc. Cary, NC, USA). All tests were two-tailed.

RESULTS

Patient characteristics

Table 1 shows the social and clinical characteristics of the sample. Across the whole sample, the median DUP was 1.41 years (interquartile range (IQR) 0.35–2.81 years). The longest time to contact was 9.86 years, but 90% had DUP shorter than 5 years. The average age at onset in the full sample was 27.2 years (standard deviation (SD) = 7.8), whereas the average age at contact was 28.9 years (SD = 7.9). The sample was predominantly male (70%), of single/separated/divorced/widowed marital status (69%), of school education and lower (80%), of monthly

TABLE 1. Patient social and clinical characteristics

Total sample (n = 421)		
DUP in years		
Mean (SD)	1.89 (1.86)	
Median (IQR)	1.41 (0.35–2.81)	
Age at onset		
Mean (SD)	27.2 (7.8)	
Median (IQR)	26 (22–30)	
Age at contact		
Mean (SD)	28.9 (7.9)	
Median (IQR)	28 (23–32)	
Gender	N	%
Female	128	30.51
Male	293	69.49
Social status	N	%
Married	131	31.23
Single and other	290	68.77
Education	N	%
School or lower	332	79.90
University or higher	84	20.10
N Missing = 5		
Monthly income	N	%
8000 SR or higher	167	40.0
Lower than 8000 S	251	60.0
N Missing = 3		
Employment	N	%
No	266	63.20
Yes	155	36.80
Family size	N	%
1–8 members	253	60.49
More than 8	165	39.51
N Missing = 3		
Living status	N	%
Alone or other	36	8.52
With family	383	91.48
N Missing = 2		
Pathway to care	N	%
Non-psychiatric and psychiatric health profession	167	39.81
Traditional healer and other	253	60.19
N missing = 1		
Drug abuse	N	%
No	347	82.32
Yes	74	17.68

DUP, duration of untreated psychosis; IQR, interquartile range; SD, standard deviation; in Social status, 'Single and Other' includes Single, Divorced, Separated and Widow; in Living Status, 'Alone and Other' includes Alone, Prison, Social Institution and other; in Pathway To Care, 'Traditional Healer and Other' includes Traditional Healer, Religious Person.

TABLE 2. Wilcoxon rank-sum test results showing factors predicting duration of untreated psychosis

Predictor	P-value
Gender	0.44
Social status	0.02
Education	0.002
Monthly income	0.02
Family size	0.21
Employment	0.88
Living status	0.75
Pathway to care	<0.0001
Schizophrenia	0.91
Drug abuse	0.70

income less than 8000 SR (60%), of no employment (63%), of 1–8 family members (60%), of living with family (91%). Only 40% had first contact through a health professional (non-psychiatric and psychiatric), 83% had schizophrenia and only 18% reported drug abuse.

Univariable associations between DUP and socio-demographic variables

To investigate the association between DUP and the categorical variables, a Wilcoxon rank-sum test was conducted and the results are shown in Table 2. Single marital status, higher education and higher monthly income show strong associations (statistically significant at the $P < 0.05$ level) with shorter DUP. Pathway to care (i.e. consulting a traditional healer) showed a strong and statistically significant (at the $P < 0.05$ level) association with longer DUP. For the continuous variable, age at onset, the Pearson correlation coefficient was –0.12 (a low negative association), between age at onset and log (DUP) with a P-value of 0.013.

Univariable analysis using Kaplan–Meier curves, log-rank tests and Wilcoxon tests

The association between DUP and other variables (except age at onset) was further investigated through Kaplan–Meier curves with log-rank and Wilcoxon tests. Table 3 shows that social status, education and pathway to care are associated with DUP and had P-values of <0.05. Monthly income and family size are weakly associated with DUP. Monthly income had a P-value of <0.05, but family size had a P-value of 0.21; this was therefore included in the multivariable model but was not a statistically significant univariable association. The Kaplan–Meier survival curves in Figures 1–3 show a clear divergence in the survival probability (here the event is the contact to services) according to social status, education and pathway to care. It is notable that the groups of single and other, of university or higher education and of initial pathway to care through health professional have a shorter DUP than their counterparts.

There was no evidence of an association between DUP and any of the other variables considered: gender, employment, living status and drug abuse. Thus, these were not included in the multivariable Cox regression analysis.

Multivariable results: Cox proportional hazards regression

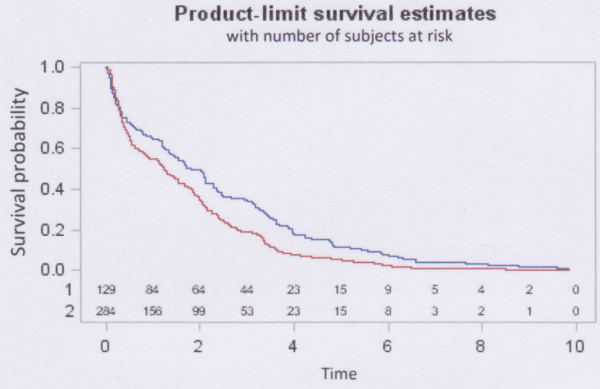
As above, a univariate Cox regression was performed for the following variables: age at onset, social status, education, pathway to care, monthly income and family size. All of their P-values were smaller than the chosen cut-off P-value of 0.2525 for entry into the multivariable model. Among them, social status, education and pathway to care were statistically significant (P-value < 0.05), so were included in the multivariate model first. Then, the model AICc was compared after adding/eliminating age at onset, monthly income, family size. The final model with the smallest AICc had the predictors of age at onset, social status, education and pathway to care. Monthly income and family size were dropped in the final model somewhat expectedly as there was collinearity between social status and family size and between education and monthly income. The unadjusted and adjusted HR and corresponding 95% CI, P-values, are shown in Table 4. All of the four predictors included in the final model are strongly associated with DUP. The adjusted HR = 1.02 for age at onset indicates that, overall, every year older at onset increases the risk of contact with services by 2% per year. After adjusting for other confounders, married status decreases the risk of contact by 33% within a year compared with single or other. After adjusting, education of school leaving level or lower decreases the risk of contact within a year by 31% compared with people with university or higher education. On the contrary, after adjusting, the pathway to care of initial contact with a health profession increases the risk of contact within a year by 69% compared with the pathway to care by traditional healer and other. Thus, older age at onset, single marital status and higher educational level were associated with shorter DUP. Long DUP was associated with help seeking from traditional healers.

TABLE 3. Log-rank test and Wilcoxon test

	Log-rank test			Wilcoxon test		
	χ^2	d.f.	P-value	χ^2	d.f.	P-value
Gender	0.4	1	0.53	0.59	1	0.44
Social status	10.12	1	0.002	5.37	1	0.02
Education	14.94	1	0.0001	10.44	1	0.001
Monthly income	3.62	1	0.06	5.78	1	0.02
Employment	0.19	1	0.66	0.02	1	0.88
Family size	2.8	1	0.09	1.56	1	0.21
Living status	0.17	1	0.68	0.12	1	0.73
Pathway to care	23.2	1	<0.0001	17.77	1	<0.0001
Drug abuse	0.02	1	0.89	0.14	1	0.71

d.f., degrees of freedom.

FIGURE 1. Survival curves for duration of untreated psychosis, stratified by social status: (——) married; (——) single and other.



DISCUSSION

Summary of results

This study is one of the largest investigations of DUP and associated variables in the Arabic world. It was conducted in all governmental hospitals to cover the whole area of Riyadh. The DUP was associated with certain demographic factors, that is, age, marital status and education level. It was also associated with help seeking from traditional healers. Other factors including nationality, gender, income, living status, family size, employment status, monthly income and history of drug abuse were not predictive.

Methodological issues

Methodological weaknesses

As the study is retrospective, the available information was extracted from case records; this method is in line with previous studies.[17,18] A study by Morgan et al. was conducted to test the clinical and social determinants of DUP. In that study, key information data were available for part of the sample from interview with patients and relatives in addition to the case records (66.3%); however, for the other part of the sample, the only available information was extracted from the medical records (33.7%). A comparison between the two parts of the sample was

FIGURE 2. Survival curves for duration of untreated psychosis, stratified by education: (——) school or lower; (——) university of higher.

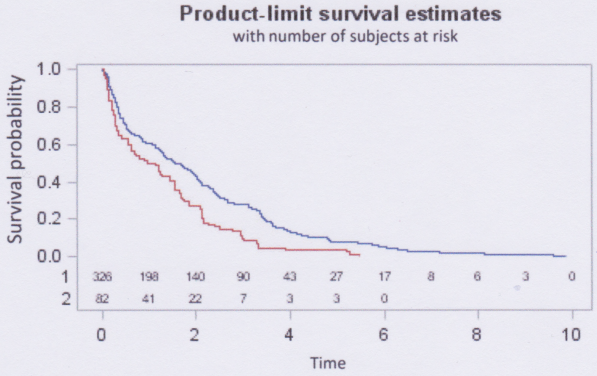
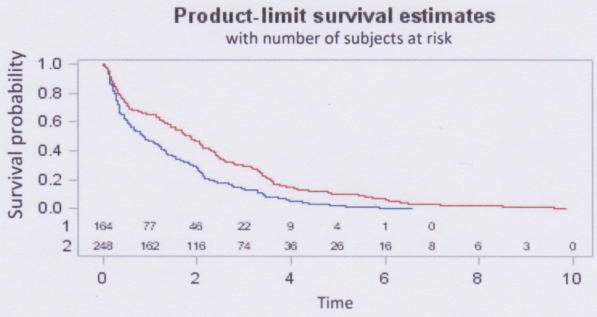


FIGURE 3. Survival curves for duration of untreated psychosis, stratified by pathway to care: (——) non-psychiatric and psychiatric health profession; (——) traditional healer and other.



carried out testing for differences in age, gender, living circumstances, social status, education, employment, mode of onset and diagnosis, and there was no evidence of any systematic information bias so that DUP could be established for both samples.[6]

It would have been very interesting and informative to test the factors that influenced time to help seeking from traditional healers, but unfortunately, the date of first seeing a traditional healer was not generally recorded so this was not possible in this study.

Similarly, a detailed examination of severity and DUP would be useful, particularly investigating change in severity during the time without treatment.

Methodological strengths

Unlike many studies, this study included not only admitted patients but also all patients who made contact with any mental health services even if not admitted within the time frame of the study, which reduced selection bias. Private hospitals only provide outpatient services in Riyadh for psychiatry. They were contacted for the purpose of this study. Unfortunately, they did not allow access to patient files to collect data. However, they indicated that most schizophrenia cases are not new, that they have been seen before in governmental hospitals or clinics. We are therefore reasonably confident that coverage was as complete as possible. In addition,

TABLE 4. Unadjusted and adjusted HR for duration of untreated psychosis (DUP)

Predictor	Unadjusted HR	(95% CI)	P-value	Adjusted HR	(95% CI)	P-value
Age at onset (per year)	1.01	(1.00, 1.03)	0.063	1.02	(1.01, 1.04)	0.002
Social status						
Married versus single or other	0.71	(0.58, 0.88)	0.002	0.67	(0.54, 0.84)	0.0004
Education						
School or lower versus university or higher	0.62	(0.48, 0.79)	0.0001	0.69	(0.54,0.89)	0.004
Pathway to care						
Non-psychiatric and psychiatric health profession versus traditional healer and other	1.64	(1.34, 2.01)	<.0001	1.69	(1.37, 2.08)	<.0001

Note: The association of monthly income and family size with DUP in the univariate Cox regression was also investigated. Unadjusted HR (95% CI) and P-value for monthly income (8000 SR or higher vs. lower than 8000 SR) were 1.19 (0.97, 1.45) and 0.09, and for family size (1–8 members vs. more than 8) were 0.88 (0.72, 1.08) and 0.21.
CI, confidence interval; HR, hazard ratio.

diagnostic objectivity was maximized by using OPCRIT checklist and associated computer diagnoses.

Comparisons with previous studies

Median DUP

We found that the median DUP of patients from Riyadh was 1.41 years (IQR 0.35–2.81 years), which is shorter than that reported by Fawzi et al. in their study (3.2 and 3.1 years for the Egyptian and Saudi patients, respectively).[7] The reason for this may be the end of DUP definition that we have adopted in our study, that is, any contact with services, whereas Fawzi defined the end of the DUP as 'the time of receiving first adequate treatment'; this might have given a shorter DUP median in our study. However, the median in our study is very long compared with those recently reported from Western countries. Archie et al. reported a median DUP of 22 weeks;[19] Drake et al. reported that the median DUP was 12 weeks.[20] On the contrary, our findings are similar to other Western studies from one to decades ago that reported that the median DUP was 1–2 years.[1–3]

Age

In this study wherein 421 psychiatric records of patients were verified and analysed, it appears that the most frequent DUP is less than 5 years (90%). The longest time to contact was 9.86 years. Adjusted HR = 1.02 for age at onset indicates that overall every year older at onset increases the risk of contact with services by 2% which means a shorter DUP. This is consistent with a recent study which showed that adolescents had a longer DUP (179 days) than adults (81 days).[21] The delays in identifying psychosis among adolescents can be understandable for a number of reasons. Firstly, some families consider psychosis symptoms as part of teenage behaviours or just a reaction to pressures and stress which might lead adolescents to be referred to teachers or social services rather than seeking help from a psychiatrist.[21] Secondly, adolescent psychosis usually presents with a slow and insidious onset, therefore early recognition of the disorder can be very difficult.[22,23] Thirdly, teenagers may be more hesitant to see psychiatrists, therefore delaying diagnosis and treatment of the disease.[24] Other studies showed no association between DUP and age.[20,25]

Help provider

Patients who sought psychiatric help from mental health professionals or other medically trained professionals are more likely to have a shorter DUP. On the contrary, those who sought help from traditional healers first appear to have longer DUP. It sometimes takes 5–10 years to treat the illness medically after an initial approach to traditional healers (n = 59). The findings show that seeking help first from traditional healers is more common in our sample (60%) compared with seeking help from a health professional (40%). This is consistent with previous findings that showed that the traditional healer was the most frequent help-seeking first contact in both Egyptian and Saudi samples.[7] Other studies from developing countries showed similar results such as Chilae et al. in Mzuzu (n = 140), 60% of the patients sought help initially from traditional healers whereas only 28% sought help from hospitals.[26] Burns et al. showed that a longer DUP is associated with spiritual attribution and seeking help from traditional healers.[9]

Saudi society tends to explain the sudden disturbed behaviour that appears in a person to be the result of witchcraft, evil eye and demonic possession

rather than scientifically explained as 'mental illness'. Jinn (demons), Sihr (magic) and Al-Ein or Nafs (evil eye) are all mentioned in the Holy Qur'an and that explains why they are mostly accepted in society.[14] As a result of these beliefs, the recognition of mental illness can be delayed, which has been claimed to affect the disease progress and treatment.[27]

It is important to point out that traditional healing is a major legal health system in Saudi Arabia. About 50–70% of psychiatric outpatients have sought help from a traditional healer at some point of their illness; 21–50% did that before even being seen by a psychiatrist.[28,29] In an early study, about 60% of psychotic outpatients had been to a traditional healer before seeking help from a psychiatrist.[30] This is in contrast to studies from Western countries, where the largest number of patients usually contact a physician first.[31]

A pilot study was conducted with 45 male traditional healers in Saudi Arabia to describe the narrated symptom pattern (psychological, physical and other symptoms caused by supernatural entities) and treatments given by them. The study revealed that traditional healers could not distinguish psychiatric symptoms and consider them to be symptoms of jinn possession, evil eye and magic. This misunderstanding is due to the lack of awareness of psychotic illnesses and their symptoms, signs and treatment.[32]

Traditional healers have a vital role in the early diagnosis of psychosis as many patients seek help from them before seeking any medical help. Therefore, it may be helpful if psychiatrists offer some training sessions, education and workshops for traditional healers in order to help them better understand and distinguish the psychosis symptoms and signs. This will help reduce the time lost before seeking professional help.

Gender

In terms of gender, there were more men (n = 287) than women (n = 126) in this study and gender was not significantly associated with DUP. Previous studies have had mixed findings. One study showed that women had a longer DUP.[32] However, several studies have shown evidence of a longer DUP in male.[7,33,34] Other studies did not find an association between gender and DUP.[20,25] A systematic review was conducted to assess the influence of gender on DUP; 27 studies (4721 patients) were included in this study. The results showed that no differences existed between male and female with regard to DUP length.[35]

Marital status

Those who were married were more likely to have a longer DUP when compared with those who were single and other (divorced, separated and widowed). This contrasts with a previous study, which showed that single patients had a longer DUP than married patients.[36] However, other studies did not show any association between marital status and DUP.[10,16] Our result might be understood by considering the impact of culture on decision making to seek treatment. This might be influenced by lack of awareness of mental illness and stigma. The decision to seek treatment is often made by the family and not by the individual,[37] and if the patient is the wife, the husband is the one who decides whether to seek treatment or not as he has authority in Arab families.[38,39] The negative impact of mental illness on the family affiliation to the community and the feeling of shame may delay treatment seeking.[37] The husband might think it good is for the family to keep the wife's illness as a secret in order not to affect their reputations in the society, which could affect the marriage of their children.

Educational level

Chen et al. said that educational level is an important tool for early detection of psychosis.[40] This study shows a higher DUP patients in 'school education and lower' category than for 'university education and higher'. However, it is not clear if being unable to finish standard level of education leads to a long DUP or long DUP increases school withdrawal and affects function negatively.

IMPLICATIONS AND LIMITATIONS

Implications

People in Arabic countries, who are developing psychosis for the first time, have a longer duration of untreated psychosis than people in Western countries.

It might be possible to educate Arabic society about the important role of psychiatrists and the services they provide and this might reduce the stigma of mental illness. This, in turn, might reduce the duration of untreated psychosis.

Limitations

The number of cases is limited, and the results are based on 421 psychiatric records.

In terms of data validity, the researcher relied upon the data retrieved from the hospitals records.

The study is focused on only one area, which is Riyadh, the capital of Saudi Arabia and one specific time, therefore the findings may not apply to other areas.

CONCLUSION

Although taking into account the limitations of the study, DUP tends to be long in Saudi Arabia, which is a major clinical concern. Seeking help from a traditional healer was a significant predictor of a long DUP. Younger age, married status and lower education level were the only demographic factors associated with a longer DUP.

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REFERENCES

1. McGlashan TH. Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course? Biol Psychiatry 1999; 46: 899–907.
2. Barnes TRE, Hutton SB, Chapman MJ, Mutsatsa S, Puri BK, Joyce EM. West London first-episode study of schizophrenia: clinical correlates of duration of untreated psychosis. Br J Psychiatry 2000; 177: 207–11.
3. Ho B, Andreasen NC, Flaum M, Nopoulos P, Miller D. Untreated initial psychosis: its relation to quality of life and symptom remission in first-episode schizophrenia. Am J Psychiatry 2000; 157: 808–15.
4. Malla AK, Norman RM, Manchanda R et al. One year outcome in first episode psychosis: influence of DUP and other predictors. Schizophr Res 2002; 54: 231–42.
5. Rosen K, Garety P. Predicting recovery from schizophrenia: a retrospective comparison of characteristics at onset of people with single and multiple episodes. Schizophr Bull 2005; 31: 735–50.
6. Morgan C, Abdul-Al R, Lappin JM et al. Clinical and social determinants of duration of untreated psychosis in the AESOP first-episode psychosis study. Br J Psychiatry 2006; 189: 446–52.
7. Fawzi M, El-Amin H, Fawzi M. Duration of untreated psychosis in two Arab samples from Egypt and Saudi Arabia: clinical and sociocultural correlates. Middle East Curr Psychiatry 2011; 18: 217–25.
8. Sharifi V, KermaniRanjbar T, Amini H, Alaghband RJ, Salesian N, Seddigh A. Duration of untreated psychosis and pathways to care in patients with first-episode psychosis in Iran. Early Interv Psychiatry 2009; 3: 131–6.
9. Burns JK, Jhazbhay K, Emsley RA. Causal attributions, pathway to care and clinical features of first-episode psychosis: a South African perspective. Int J Soc Psychiatry 2011; 57: 538–45.
10. Naqvi HA, Hussain S, Zaman M, Islam M. Pathways to care: duration of untreated psychosis from Karachi, Pakistan. PLoS ONE 2009; 4: e7409.
11. Jones PB, Bebbington P, Foerster A et al. Premorbid social underachievement in schizophrenia. Results from the Camberwell Collaborative Psychosis Study. Br J Psychiatry 1993; 162: 65–71.
12. McGorry PD. A stitch in time the scope for preventive strategies in early psychosis. Eur Arch Psychiatry Clin Neurosci 1998; 248: 22–31.
13. Vogel D, Wade N, Wester S, Larson L, Hackler A. Seeking help from a mental health professional: the influence of one's social network. J Clin Psychol 2007; 63: 233–45.
14. Al-Subaie A, Al-Hamad A. Psychiatry in Saudi Arabia. In: Al-Issa I, ed. Al-Junun: Mental Illness in the Islamic World. Madison, CT: International Universities Press, 2000; 205–33.
15. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva, 1992.
16. Craig TJ, Bromet EJ, Fenning S, Tanenberg-Karant M, Lavelle J, Galambos N. Is there an association between duration of untreated psychosis and 24-month clinical outcome in a first-admission series? Am J Psychiatry 2000; 157: 60–6.
17. Primavera D, Bandecchi C, Lepori T, Sanna L, Nicotra E, Carpiniello B. Does duration of untreated psychosis predict very long term outcome of schizophrenic disorders? Results of a retrospective study. Ann Gen Psychiatry 2012; 11: 1–6.
18. Thomas SP, Nandhra HS. Early intervention in psychosis: a retrospective analysis of clinical and social factors influencing duration of untreated psychosis. Prim Care Companion J Clin Psychiatry 2009; 11: 212.
19. Archie S, AkhtarDanesh N, Norman R, Malla A, Roy P, Zipursky RB. Ethnic diversity and pathways to care for a first episode of psychosis in Ontario. Schizophr Bull 2010; 36: 688–701.
20. Drake R, Haley CJ, Akhtar S, Lewis SW. Causes and consequences of duration of untreated psychosis in schizophrenia. Br J Psychiatry 2000; 177: 511–5.
21. Dominguez MD, Fisher HL, Major B et al. Duration of untreated psychosis in adolescents: ethnic differences and clinical profiles. Schizophr Res 2013; 150: 526–32.
22. Rosen JL, Miller TJ, D'Andrea JT, McGlashan TH, Woods SW. Comorbid diagnoses in patients meeting criteria for the schizophrenia prodrome. Schizophr Res 2006; 85: 124–31.
23. Hollis C. Adolescent schizophrenia. Adv Psychiatr Treat 2000; 6: 83–92.
24. De Haan L, Welborn K, Krikke M, Linszen DH. Opinions of mothers on the first psychotic episode and the start of treatment of their child. Eur Psychiatry 2004; 19: 226–9.
25. Shrivastava A, Shah N, Johnston M, Stitt L, Thakar M, Chinnasamy G. Effects of duration of untreated psychosis on long-term outcome of people hospitalized with first episode schizophrenia. Ind J Psychiatry 2010; 52: 164–7.
26. Chilae H, Banda R, Muyawa J, Kaminga A. Duration of untreated psychosis and associated factors in first episode psychosis in Mzuzu in Northern Malawi. Afr J Psychiatry 2014; 17: 503–7.
27. El-Islam MF. Arab culture and mental health care. Transcult Psychiatry 2008; 45: 671–82.
28. Hussein F. A study of the role of unorthodox treatments of psychiatric illnesses. Arab J Psychiatry 1989; 2: 170–84.
29. Al-Sabaie A. Psychiatry in Saudi Arabia: an overview. Psychiatr Bull 1990; 14: 298–300.
30. Okasha A, Kamel M, Hassan AH. Preliminary psychiatric observations in Egypt. Br J Psychiatry 1968; 114: 949–55.
31. Anderson K, Fuhrer R, Mall A. The pathways to mental health care of first-episode psychosis patients: a systematic review. Psychol Med 2010; 40: 1585–97.
32. Al-Habeeb TA. A pilot study of faith healers on evil eye, jinn possession, and magic in the Kingdom of Saudi Arabia. J Fam Community Med 2003; 10: 31.

33. Koste A, Lajer M, Lindhard A, Rosenbaum B. Gender differences in first episode psychosis. Soc Psychiatry Psychiatr Epidemiol 2008; 43: 940–6.
34. Larsen TK, McGlashan TH, Moe LC. First-episode schizophrenia. Schizophr Bull 1996; 22: 241–56.
35. Thorup A, Petersen L, Jeppesen P et al. Gender differences in young adults with first -episode schizophrenia spectrum disorders at baseline in the Danish OPUS study. J Nerv Ment Dis 2007; 195: 396–405.
36. Pek E, Mythily S, Chong S. Clinical and social correlates of duration of untreated psychosis in first-episode psychosis patients. Ann Acad Med Singapore 2006; 35: 24–6.
37. Okasha A. Focus on psychiatry in Egypt. Br J Psychiatry 2004; 185: 266–72.
38. Morsy SA. Gender, Sickness, and Healing in Rural Egypt: Ethnography in Historical Context. Boulder, CO: San Francisco CA/Oxford: Westview Press, 1993.
39. Shalhoub-Kevorkian N. Law, politics, and violence against women: a case study of Palestinians in Israel. Law Policy 1999; 21: 189–211.
40. Chen EYH, Dunn ELW, Miao MYK et al. The impact of family experience on the duration of untreated psychosis (DUP) in Hong Kong. Soc Psychiatry Psychiatr Epidemiol 2005; 40: 350–6.